

### This week in therapeutics

| Indication    | Target/marker/pathway | Summary  | Licensing status   | Publication and contact information  |
|---------------|-----------------------|--|--|--|
| <b>Cancer</b> |                       |  |  |  |
| Melanoma      | IGFBP7                | <p>A study in cell culture and xenograft mice suggests that the secreted protein IGFBP7 could be useful for treating melanomas with <i>BRAF</i> activating mutations. Activating mutations in <i>BRAF</i> serine/threonine protein kinase are frequent in melanoma, resulting in uncontrolled tumor proliferation. In xenograft mice, systemic administration of recombinant IGFBP7 suppressed the growth of BRAFV600E tumors. In addition, human melanoma samples with activated <i>BRAF</i> lacked detectable levels of IGFBP7, whereas melanomas lacking activated <i>BRAF</i> expressed IGFBP7. In the mice, IGFBP7 expression was downregulated as a result of epigenetic silencing involving promoter hypermethylation. Next steps include scaling up production of IGFBP7 for additional testing and toxicology studies.</p> <p>Roche has an exclusive worldwide license from Plexikon Inc. to develop and commercialize PLX4032, a small-molecule inhibitor of the oncogenic V600E mutation in the <i>BRAF</i> gene. The compound is in Phase I testing to treat cancer.</p> | <p>Patent application filed for the use of IGFBP7 to treat <i>BRAF</i>-positive melanoma and other <i>BRAF</i>-positive malignancies; unlicensed</p> | <p>Wajapeyee, N. <i>et al. Cell</i>; published online Feb. 8, 2008; doi:10.1016/j.cell.2007.12.032<br/> <b>Contact:</b> Michael R. Green, Howard Hughes Medical Institute, University of Massachusetts, Medical School, Worcester, Mass.<br/>                     e-mail: <a href="mailto:michael.green@umassmed.edu">michael.green@umassmed.edu</a></p> |