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THE DISTILLERY

This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Cancer				
Chronic myelogenous leukemia (CML)	β-Catenin (CTNNB1); interferon regulatory factor 8 (IRF8)	*In vitro* and mouse studies suggest simultaneously increasing *IRF8* expression and inhibiting CTNNB1 could help treat CML. In *Irf8*$^{-/-}$ mice, which develop CML, enhanced activation of Ctnnb1 caused disease progression to fatal blast crisis. In a BCR-ABL tyrosine kinase mouse model of CML, combined *Irf8* knockout and Ctnnb1 activation increased Gleevec imatinib resistance compared with wild-type *Irf8* expression and normal Ctnnb1 activation. Next steps include testing Gleevec in combination with *Irf8* activation and Ctnnb1 inhibition as a triple therapy at the initiation of blast crisis in models of CML. Novartis AG markets Gleevec, a BCR-ABL tyrosine kinase inhibitor, to treat gastrointestinal stromal tumors (GISTs), acute lymphoblastic leukemia (ALL) and CML. Prism Pharma Co. Ltd. and Eisai Co. Ltd. have the CTNNB1 inhibitor PRI-724 in Phase I/II testing to treat CML and other cancers. Marina Biotech Inc.'s CEQ508, an oral RNAi targeting CTNNB1, is in Phase I/II testing to treat colorectal cancer.	Patent and licensing status not applicable	Scheller, M. *et al. J. Exp. Med.*; published online Oct. 7, 2013; doi:10.1084/jem.20130706 **Contact:** Achim Leutz, Max Delbrueck Center for Molecular Medicine, Berlin, Germany e-mail: aleutz@mdc-berlin.de **Contact:** Marina Scheller, same affiliation as above e-mail: m.scheller@uke.de

SciBX 6(43); doi:10.1038/scibx.2013.1220
Published online Nov. 7, 2013