

This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Cancer				
Chronic myelogenous leukemia (CML)	Janus kinase-2 (JAK-2); signal transducer and activator of transcription 5 (STAT5)	<p>Cell culture and mouse studies suggest JAK-2 inhibitors exert anti-CML effects via off-target activity at STAT5. JAK-2 has been implicated as a target in CML because the kinase activates STAT5, a key driver of leukemia. However, in a mouse model of CML, deletion of <i>Jak-2</i> had no effect on survival compared with normal <i>Jak-2</i> expression. In leukemia cell lines treated with a panel of JAK-2 inhibitors known to decrease leukemia cell growth, deletion of <i>Jak-2</i> did not affect IC₅₀ values, suggesting the compounds work via off-target effects on STAT5. Next steps include developing therapeutics that directly target STAT5.</p> <p>Jakafi, an oral JAK-1 and JAK-2 inhibitor from Incyte Corp. and Novartis AG, is approved to treat myeloproliferative disorders and is in Phase II trials to treat relapsed and refractory leukemia, including CML.</p> <p>At least seven other companies have compounds that inhibit JAK-2 in Phase II trials or earlier to treat various indications including myeloproliferative disorders.</p> <p>SciBX 5(6); doi:10.1038/scibx.2012.146 Published online Feb. 9, 2012</p>	Unpatented; licensing status not applicable	<p>Hantschel, O. <i>et al. Nat. Chem. Biol.</i>; published online Jan. 29, 2012; doi:10.1038/nchembio.775</p> <p>Contact: Giulio Superti-Furga, Austrian Academy of Sciences, Vienna, Austria e-mail: gsuperti-furga@cemm.oeaw.ac.at</p> <p>Contact: Veronika Sexl, University of Veterinary Medicine Vienna, Vienna, Austria e-mail: veronica.sexl@vetmeduni.ac.at</p>