This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Cancer				
Chronic lymphocytic leukemia (CLL); mantle cell lymphoma (MCL); multiple myeloma (MM)	Endoplasmic reticulum to nucleus signaling 1 (ERN1; IRE1); Bruton's tyrosine kinase (Btk)	<p>Cell culture and mouse studies suggest inhibiting IRE1 and Btk could help treat CLL, MCL and MM. Chemical synthesis and <i>in vitro</i> testing of chromenone analogs identified compounds that inhibited the activity of IRE1's RNase domain with nanomolar to low micromolar potency. In a transgenic mouse model of CLL, one lead inhibitor decreased CLL cell levels in peripheral blood compared with vehicle. In CLL cells from the mouse models and human CLL, MCL and MM cell lines, the IRE1 inhibitor plus the Btk inhibitor Imbruvica ibrutinib caused more potent growth inhibition than either agent alone. Ongoing work includes testing IRE1 inhibitors and ibrutinib in mouse models of B cell lymphoma.</p> <p>Pharmacyclics Inc. and Johnson & Johnson market Imbruvica to treat CLL and MCL. The compound is in Phase III testing to treat B cell lymphoma and non-Hodgkin's lymphoma (NHL) and Phase II testing to treat MM and lymphoma. Celgene Corp. has the covalent small molecule Btk inhibitor AVL-292 (CC-292) in Phase I testing to treat CLL and B cell lymphoma. Ono Pharmaceutical Co. Ltd. has the Btk inhibitor ONO-4059 in Phase I testing to treat B cell lymphoma.</p> <p>SciBX 7(24); doi:10.1038/scibx.2014.702 Published online June 19, 2014</p>	For findings from both studies, patent application filed by the H. Lee Moffitt Cancer Center & Research Institute; available for licensing	<p>Ranatunga, S. <i>et al. J. Med. Chem.</i>; published online April 21, 2014; doi:10.1021/jm5002452</p> <p>Tang, C.-H.A. <i>et al. J. Clin. Invest.</i>; published online May 8, 2014; doi:10.1172/JCI73448</p> <p>Contact: Chih-Chi Andrew Hu, H. Lee Moffitt Cancer Center & Research Institute, Tampa, Fla. e-mail: chih-chi.hu@moffitt.org</p> <p>Contact: Juan R. Del Valle, same affiliation as above e-mail: juan.delvalle@moffitt.org</p>