This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Cancer				
Cancer	BCL2-associated X protein (BAX); BCL2-antagonist/killer 1 (BAK1; BAK); B cell lymphoma 2 (BCL-2; BCL2); BCL2 homology domain 3 (BH3)	<p>Structural studies have identified regions of BAK that could guide the development of apoptosis-inducing compounds that could help treat cancer. Crystal structures of BCL2 have guided the development of BH3-mimetic compounds that bind and inhibit prosurvival proteins, but it was unclear how the BH3 domains bind and activate distinct proapoptotic proteins, including BAX and BAK. <i>In vitro</i>, full-length BAK protein was purified and photochemical crosslinking identified a BH3 binding site on BAK that was structurally distinct from the BH3 binding site of BAX. Ongoing work includes optimizing the potency and specificity of BAX and BAK modulators. Abbott Laboratories and Roche's Genentech Inc. have navitoclax (ABT-263), a pan-inhibitor of BCL2-family proteins, in Phase I/II testing for small cell lung cancer and Phase I testing for other cancers.</p> <p>At least six other companies have antagonists of BCL2-family proteins in Phase II testing or earlier to treat various cancers.</p> <p>SciBX 6(8); doi:10.1038/scibx.2013.188 Published online Feb. 28, 2013</p>	<p>Stapled BH3 peptides that directly engage BAX, BAK and antiapoptotic BCL-2 family targets patented; licensed to Aileron Therapeutics Inc.; small molecules that directly engage BAX patented; available for licensing</p>	<p>Leshchiner, E.S. <i>et al. Proc. Natl. Acad. Sci. USA</i>; published online Feb. 12, 2013; doi:10.1073/pnas.1214313110 Contact: Loren D. Walensky, Dana-Farber Cancer Institute, Boston, Mass. e-mail: loren_walensky@dfci.harvard.edu</p>