This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Neurology				
Rett syndrome	DNA (cytosine-5-)-methyltransferase 1 (DNMT1); 3-phosphoinositide dependent protein kinase-1 (PDPK1); aurora kinase A (AURKA; aurora-A); X inactive specific transcript (XIST); methyl CpG binding protein 2 (MECP2; RTT)	<p>Cell culture studies suggest small molecules that reactivate inactive X chromosomes could help treat Rett syndrome, which is linked to deficiencies in <i>MECP2</i>. RNAi screening in a female mouse embryonic fibroblast cell line identified <i>Dnmt1</i>, <i>Pdpk1</i>, <i>Aurka</i> and 10 other genes that upregulated Xist and thereby helped to inactivate X chromosomes. In differentiated female mouse embryonic stem cells, a PDPK1 inhibitor decreased Xist levels and increased <i>Mecp2</i> mRNA levels compared with vehicle. In fibroblast cell lines derived from a patient with Rett syndrome, inhibitors of PDPK1, DNA methyltransferase or AURKA increased expression of wild-type <i>MECP2</i> mRNA compared with vehicle. Next steps could include testing the inhibitors in mouse models of Rett syndrome.</p> <p>Takeda Pharmaceutical Co. Ltd. has alisertib (MLN8237), a second-generation AURKA inhibitor, in Phase III testing to treat T cell lymphoma, Phase II testing to treat multiple other cancers and Phase I testing to treat solid tumors.</p> <p>Otsuka Pharmaceutical Co. Ltd. has SGI-110, a small molecule DNA methyltransferase inhibitor, in Phase II testing to treat renal and ovarian cancers. The compound also is in Phase II testing to treat hematological malignancies and in Phase I testing to treat solid tumors.</p> <p>Arno Therapeutics Inc. has AR-12 (OSU-03012), a small molecule PDPK1 inhibitor, in Phase I testing to treat solid tumors and lymphoma.</p> <p>SciBX 7(35); doi:10.1038/scibx.2014.1052 Published online Sept. 11, 2014</p>	Patent and licensing status unavailable	<p>Bhatnagar, S. <i>et al. Proc. Natl. Acad. Sci. USA</i>; published online Aug. 18, 2014; doi:10.1073/pnas.1413620111</p> <p>Contact: Michael R. Green, University of Massachusetts Medical School, Worcester, Mass. e-mail: michael.green@umassmed.edu</p>