This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Cancer				
Melanoma	BRAF; platelet derived growth factor B (PDGFB; PDGF2); neuroblastoma Ras viral (v-Ras) oncogene (NRAS); MAP kinase kinase kinase 8 (MAP3K8; COT); MAP kinase kinase 1 (MAP2K1; MEK1); MAP2K2 (MEK2)	<p><i>In vitro</i> studies suggest that inhibiting PDGFB or components of the MAPK pathway could help treat BRAF⁺, drug-resistant melanoma. In BRAF⁺ human melanoma cell lines and tumor samples that were resistant to BRAF inhibitors, PDGFB and MAP3K8 were overexpressed or NRAS contained mutations that activated MEK1 and MEK2 signaling compared with what was seen in BRAF inhibitor-sensitive controls. In the drug-resistant cell lines and tumor samples, PDGFB, NRAS or MAP3K8 knockdown or inhibition of MEK1 and MEK2 decreased cell viability compared with BRAF inhibition or no treatment. Planned studies include testing PDGFB, NRAS, MAP3K8 and/or MEK1 and MEK2 inhibition in animal models of BRAF inhibitor-resistant melanoma.</p> <p>PLX4032 (R7204; RG7204), an oral small molecule inhibitor of oncogenic BRAF(V600E) from Roche and Plexxikon Inc., is in Phase III testing to treat melanoma and Phase I testing to treat colorectal cancer.</p> <p>GSK1120212, a small molecule inhibitor of MEK1 and MEK2 from GlaxoSmithKline plc, is in Phase II testing to treat previously treated BRAF(V600E)⁺ melanoma.</p> <p>ARRY-886 (AZD6244), an ATP noncompetitive MEK inhibitor from Array BioPharma Inc. and AstraZeneca plc, is in Phase II testing to treat non-small cell lung cancer (NSCLC), colorectal cancer and liver cancer.</p> <p>E10030, an aptamer targeting PDGFB from Archemix Corp. and Ophthotech Corp., is in Phase II testing to treat age-related macular degeneration.</p> <p>SciBX 3(47); doi:10.1038/scibx.2010.1410 Published online Dec. 9, 2010</p>	<p>Findings in the first study patented by the University of California; available for licensing</p> <p>Findings in the second study patented by the Dana-Farber Cancer Institute and the Broad Institute of MIT and Harvard; licensing status undisclosed</p>	<p>Nazarian, R. <i>et al. Nature</i>; published online Nov. 24, 2010; doi:10.1038/nature09626 Contact: Roger S. Lo, University of California, Los Angeles, Calif. e-mail: rlo@mednet.ucla.edu</p> <p>Johannessen, C.M. <i>et al. Nature</i>; published online Nov. 24, 2010; doi:10.1038/nature09627 Contact: Levi A. Garraway, Dana-Farber Cancer Institute, Boston, Mass. e-mail: Levi_Garraway@dfci.harvard.edu</p>