This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Cancer				
Acute myelogenous leukemia (AML)	DNA (cytosine-5-)-methyltransferase 3α (DNMT3A) R882H	<i>In vitro</i> studies suggest targeting DNMT3A R882H could be useful for treating AML. The R882H mutation in DNMT3A is commonly found in AML, but the functional consequence of this mutation has been unclear. A series of cellular assays showed that DNMT3A R882H had 80% lower methyltransferase activity than wild-type DNMT3A and resulted in greater than expected loss of global DNA methylation when coexpressed with wild-type enzyme. In a human cell line, coexpression of R882H-mutant and wild-type DNMT3A showed that the mutant inhibits the wild-type enzyme by blocking its ability to form active tetramers, suggesting the R882H mutation acts in a dominant-negative manner. Next steps could include developing pharmacological agents that block the dominant-negative activity of DNMT3A R882H without affecting the wild-type methyltransferase.	Patent and licensing status unavailable	Russler-Fermain, D.A. <i>et al. Cancer Cell</i> ; published online March 18, 2014; doi:10.1016/j.ccr.2014.02.010 Contact: Timothy J. Ley, Washington University in St. Louis, St. Louis, Mo. e-mail: timley@wustl.edu
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