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THE DISTILLERY

This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Cancer				
B cell lymphoma	B cell lymphoma 2 (BCL-2; BCL2); cyclin dependent kinase 4 (CDK4); cyclin dependent kinase inhibitor 2A (CDKN2A; INK4a; ARF; p16INK4a); CDKN2B (INK4B; MTS2); retinoblastoma 1 (RB1)	Patient and mouse studies suggest combined inhibition of CDK4 and BCL2 could help treat high-risk follicular lymphomas with mutations in the retinoblastoma pathway. In patients with indolent follicular lymphoma, genomic alterations in members of the retinoblastoma pathway including *CDKN2A*, *CDKN2B*, *RB1* and *CDK4* were associated with high-risk disease. In mouse xenograft models of follicular lymphoma with elevated RB1 phosphorylation, a combination of small molecule inhibitors of CDK4 and BCL2 decreased tumor growth compared with either inhibitor alone. Next steps could include evaluating the combination in additional types of B cell lymphomas with mutations in the retinoblastoma pathway. Pfizer Inc. and Amgen Inc. have the oral small molecule CDK4 and CDK6 inhibitor PD-0332991 in Phase III testing to treat breast cancer. Novartis AG and Otsuka Pharmaceutical Co. Ltd. have the CDK4 and CDK6 inhibitor LEE011 in Phase III testing for the same indication. At least two other companies have dual inhibitors of CDK4 and CDK6 in Phase II or earlier testing to treat various cancers. At least 12 companies have BCL2 inhibitors in Phase II or earlier testing to treat various cancers.	Patent and licensing status unavailable	Oricchio, E. *et al. J. Exp. Med.*; published online June 9, 2014; doi:10.1084/jem.20132120 **Contact:** Hans-Guido Wendel, Memorial Sloan-Kettering Cancer Center, New York, N.Y. e-mail: wendelh@mskcc.org

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