TARGETING THE BRAF V600E MUTATION IN MULTIPLE MYELOMA


Précis: A patient with BRAF V600E-mutant multiple myeloma experienced a rapid, stable response to the BRAF inhibitor vemurafenib.

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METABOLIC AND FUNCTIONAL GENOMIC STUDIES IDENTIFY DEOXYTHYMIDYLATE KINASE AS A TARGET IN LKB1-MUTANT LUNG CANCER


Précis: Inhibition of DTYMK, a critical enzyme for nucleotide metabolism, is synthetically lethal with LKB1 deficiency in KRAS-driven lung cancer.

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Précis: Inhibition of DTYMK, a critical enzyme for nucleotide metabolism, is synthetically lethal with LKB1 deficiency in KRAS-driven lung cancer.

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Curry and colleagues made the surprising observation that two adjacent tumor types with either low or high AKT activity can develop in Pten-null lungs. Heterogeneous AKT activation was cell autonomous and associated with differential expression of ectonucleoside triphosphate diphosphohydrolase 5 (ENTPD5), a UDPase that promotes receptor tyrosine kinase folding in the endoplasmic reticulum. Knockdown of ENTPD5 led to a reduction in levels of insulin growth factor receptor β (IGFIRβ), an upstream activator of AKT. In human non–small cell lung cancers (NSCLC), AKT phosphorylation was directly correlated with ENTPD5 expression, but not always with loss of PTEN expression. Together, these findings suggest that PTEN loss may not be sufficient to activate AKT and may not be an appropriate biomarker of PI3K/AKT activation or response to PI3K/AKT-targeted therapies. For details, please see the article by Curry and colleagues on page 908.