A Coding Single-Nucleotide Polymorphism in Lysine Demethylase KDM4A Associates with Increased Sensitivity to mTOR Inhibitors. . . 245


Précis: A germline coding SNP in the chromatin-modifying enzyme gene KDM4A increases its protein turnover and enhances mTOR inhibitor sensitivity, suggesting this SNP as a potential candidate biomarker in NSCLC.

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Lysine Demethylase KDM4A Associates with Translation Machinery and Regulates Protein Synthesis . . . . . . . . . . 255

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Précis: Cytoplasmic KDM4A modulates protein synthesis via interaction with the translation initiation complex, and inhibition of KDM4A/KDM5A enhances mTOR inhibitor sensitivity.

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Précis: Chronic BRAF inhibition leads to AKT–EPHA2-induced melanoma cell invasion and is associated with metastatic spread in patients treated with BRAF inhibitors.

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Correction

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ON THE COVER

Chromatin-modifying enzymes such as lysine (K)-specific demethylases (KDM) have been implicated in tumorigenesis. Van Rechem and colleagues identified a nonsynonymous coding SNP in KDM4A, which increased its protein turnover and was associated with worse outcome in non–small cell lung cancer. Reduced KDM4A expression or homozygosity for this SNP increased the sensitivity of lung cancer cells to mTOR inhibitors. In a second article, Van Rechem and colleagues found that KDM4A regulated protein synthesis by interacting with and modulating the distribution of translation initiation factors in polysome fractions. In addition, KDM4A depletion or treatment with a JmjC demethylase inhibitor enhanced the suppressive effects of mTOR inhibition on translation initiation. Together, these studies implicate KDM4A as a potential therapeutic target and a possible biomarker for mTOR inhibitor therapy. For details, please see the articles by Van Rechem and colleagues on pages 245 and 255. Cover photo by Johnathan R. Whetstine, of the sculpture Dancing Peptides by Mara Haseltine.