Oncogenic Isocitrate Dehydrogenase Mutations: Mechanisms, Models, and Clinical Opportunities

R.A. Cairns and T.W. Mak

Discovery of a Novel ERK Inhibitor with Activity in Models of Acquired Resistance to BRAF and MEK Inhibitors


Précis: An ERK1/2 inhibitor with properties of both type I and type II kinase inhibitors suppresses MAPK signaling and proliferation in BRAF and MEK inhibitor-resistant cancer cells. See commentary, p. 719

Inhibition of Ron Kinase Blocks Conversion of Micrometastases to Overt Metastases by Boosting Antitumor Immunity

H. Eyob, H.A. Ekiz, Y.S. DeRose, S.E. Waltz, M.A. Williams, and A.L. Welm

Précis: The receptor tyrosine kinase RON suppresses antitumor immune responses to promote metastatic outgrowth and is a potential therapeutic target to inhibit metastasis.

Frequent Mutation of the PI3K Pathway in Head and Neck Cancer Defines Predictive Biomarkers


Précis: PI3K pathway mutations are found in 30.5% of head and neck squamous cell carcinomas and may indicate sensitivity to PI3K inhibitors. See commentary, p. 722

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Head and neck squamous cell carcinomas (HNSCC) are a genetically heterogeneous group of cancers with a poor survival rate. Lui and colleagues evaluated the mutation frequency of mitogenic pathways in HNSCCs and found that 30.5% of tumors harbored PI3K pathway mutations. Patient-derived tumorgrafts with hotspot and noncanonical PIK3CA mutations were highly sensitive to PI3K inhibitors. Pickering and colleagues performed integrated genomic analyses of oral squamous cell carcinomas (OSCC), a particularly lethal, poorly characterized HNSCC subtype. The Notch pathway was deregulated in 66% of OSCCs, and inactivation of NOTCH1 was shown to drive OSCC growth. Common inactivating mutations of FAT1 and CASP8 were also identified. Together, these findings provide insight into the etiology of HNSCC and identify potential therapeutic targets. For details, please see the article by Lui and colleagues on page 761 and the article by Pickering and colleagues on page 770.