RESEARCH BRIEF

Suppression of STING Associated with LKB1 Loss in KRAS-Driven Lung Cancer .......... 34

Précis: Loss of LKB1 in KRAS-mutant lung cancer results in SAM-mediated activation of DNMT1 and EZH2, which subsequently represses the expression of STING and PD-L1 to promote immune escape.

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Remodeling of the Collagen Matrix in Aging Skin Promotes Melanoma Metastasis and Affects Immune Cell Motility .......... 64

Précis: Loss of the cross-linking protein HAPLN1 in skin fibroblasts during aging results in changes to the extracellular matrix architecture that enhance melanoma cell invasion but impair immune cell infiltration.

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Précis: Inactivation of Nf1 in a Hoxb7-expressing cell lineage faithfully models neurofibromagenesis and provides insights into the developmental origin of both plexiform and cutaneous neurofibroma.

Cellular Origin, Tumor Progression, and Pathogenic Mechanisms of Cutaneous Neurofibromas Revealed by Mice with Nf1 Knockout in Boundary Cap Cells ... 130
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ON THE COVER
Kitajima and colleagues found that KRAS-mutant/LKB1-null (KL) lung cancers exhibit upregulation of genes associated with oxidative stress and downregulation of genes involved in interferon signaling, including TMEM173, which encodes the dsDNA sensor STING. A screen of epigenetic inhibitors revealed that inhibiting DNMT1 and EZH2 restored STING expression in STING-low KL cell lines, and the binding of DNMT1 to the TMEM173 promoter was increased in STING-null KL cell lines compared to STING-low KL cell lines. Ectopic expression of LKB1 combined with inhibition of DNMT1 restored STING expression and pathway activation, and a STING agonist restored PD-L1 expression in KL cell lines. Collectively, these findings demonstrate that LKB1 negatively regulates STING in KRAS-driven lung cancer and suggest potential therapeutic strategies for patients with KRAS-mutant/LKB1-null lung cancer. For details, please see the article by Kitajima and colleagues on page 34.