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### RESEARCH BRIEF

- **Suppression of STING Associated with LKB1 Loss in KRAS-Driven Lung Cancer**
  
  **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.
  
  *See commentary, p. 16*

### RESEARCH ARTICLES

- **Genome-Informed Targeted Therapy for Osteosarcoma**
  
  **Précis:** Genomic characterization and the establishment of patient-derived xenografts identify therapeutic targets within recurrent SCNAs in osteosarcoma subclasses.

### VIEWS

- **In The Spotlight**
  
  - **Evading the STING: LKB1 Loss Leads to STING Silencing and Immune Escape in KRAS-Mutant Lung Cancers**
    - C.M.D. Corte and L.A. Byers
    
    *See article, p. 34*

  - **Something Old, Something New: The Tumor Microenvironment Comes of Age**
    - K.L. Marie and G. Merlino
    
    *See article, p. 64*

  - **Circulating Tumor Cells: Come Together, Right Now, Over Metastasis**
    - P. Rodrigues and S. Vanharanta
    
    *See article, p. 96*

### MINI REVIEW

- **The Biology of m5A RNA Methylation in Normal and Malignant Hematopoiesis**
  - L.P. Vu, Y. Cheng, and M.G. Kharas

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**Age-Related Changes in HAPLN1 Increase Lymphatic Permeability and Affect Routes of Melanoma Metastasis** ........................................... 82

 précis: Changes in ECM degradation and lymphatic vasculature permeability during aging are mediated by the cross-linking protein HAPLN1 and determine the route of metastatic dissemination.

See commentary, p. 19

**Homophilic CD44 Interactions Mediate Tumor Cell Aggregation and Polyclonal Metastasis in Patient-Derived Breast Cancer Models** .............................................. 96

 précis: Intercellular homophilic CD44 interaction-mediated tumor cell aggregation recruits PK2 and activates the PK2 signaling pathway to drive tumorigenesis and polyclonal metastasis.

See commentary, p. 22

**Spatiotemporal Loss of NF1 in Schwann Cell Lineage Leads to Different Types of Cutaneous Neurofibroma Susceptible to Modification by the Hippo Pathway** ........................................ 114

 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

 précis: Loss of Nf1 in Prss56-expressing boundary cap cells recapitulates both cutaneous and plexiform neurofibroma and provides insight into neurofibromagenesis.

Acknowledgment to Reviewers ........................................ 148

**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.