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### PRIORITY REPORTS

**5211** SBI-0640756 Attenuates the Growth of Clinically Unresponsive Melanomas by Disrupting the eIF4F Translation Initiation Complex
Yongmei Feng, Anthony B. Pinkerton, Laura Hulea, Tongwu Zhang, Michael A. Davies, Stefan Goetheut, Yann Cheli, Hongwei Yin, Eric Lau, Huyungsoo Kim, Surya K. De, Elisa Barile, Maurizio Pellechcia, Marcus Rosenberg, Jian-Liang Li, Brian James, Christian A. Hassig, Kevin M. Brown, Ivan Topisirovic, and Ze’ev A. Ronai
Précis: This study presents work on a first-in-class inhibitor of the translation initiation complex eIF4F, the targeting of which may offer broad therapeutic applications in cancer.

**5219** Genomic Profiling of Penile Squamous Cell Carcinoma Reveals New Opportunities for Targeted Therapy
Précis: By offering a description of the genomic alterations underlying penile squamous cell carcinoma, this study offers the first opportunity to reposition available molecular-targeted drugs for use in this disease, with immediate implications for clinical testing.

**5228** UV-Associated Mutations Underlie the Etiology of MCV-Negative Merkel Cell Carcinomas
Précis: These findings suggest how a rare but highly invasive and mainly untreatable sensory cell cancer in the skin might be managed by targeted therapeutic drugs currently available in clinic.
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5329 SLC46A3 Is Required to Transport Catabolites of Noncleavable Antibody Maytansine Conjugates from the Lysosome to the Cytoplasm
Précis: This study identifies a lysosome transporter that is essential for the antitumor effects of antibody-drug conjugates containing the cytotoxic compound maytansine, the first of which was approved recently to treat breast cancer.

5341 Identification of Variant-Specific Functions of PIK3CA by Rapid Phenotyping of Rare Mutations
Précis: A functional genomics platform integrates high-throughput gene mutagenesis and molecular barcoding technologies with functional screening to rapidly interrogate tumor mutations driving malignant phenotypes.

TUMOR AND STEM CELL BIOLOGY

5355 Targeting a Plk1-Controlled Polarity Checkpoint in Therapy-Resistant Glioblastoma-Propagating Cells
Précis: This study illuminates how heterogeneous glioblastoma cell subpopulations respond to BRAF/MAPK inhibition, highlighting cell polarity and asymmetric cell division as distinguishing features of therapy-resistant tumor-propagating cells that must be eradicated to prevent disease relapse.

5367 Disseminated Tumor Cells Persist in the Bone Marrow of Breast Cancer Patients through Sustained Activation of the Unfolded Protein Response
Kai Barkowicki, Marcel Rvianskow, Friedrich Buck, Tobias M. Gogges, Lars Nilse, Volker Ausmann, Anjke Andreas, Volkmar Müller, Harriët Wilman, Sabine Rietdorf, Hartmut Schlüter, and Klaus Pantei
Précis: These findings provide the evidence that the unfolded protein response supports the survival of disseminated tumor cells, which are under acute microenvironmental stress, with implications for defining a general predictive biomarker of metastatic relapse in cancer patients after their initial treatment.

5378 PIK3CAH1047R Accelerates and Enhances KRASG12D-Driven Lung Tumorigenesis
Shon Green, Christy L. Trejo, and Martin McMahon
Précis: Activating mutations in the PI3K lipid signaling pathway can act as secondary hits needed to potentiate the oncogenicity of mutant KRAS in the lung, providing mechanistic insights into the sequential steps governing tumor progression.

5392 Targeted Deletion of p53 in Lgr5-Expressing Intestinal Stem Cells Promotes Colon Tumorigenesis in a Preclinical Model of Colitis-Associated Cancer
Laurie A. Davidson, Evelyn S. Callaway, Eunjoo Kim, Brad R. Weeks, Yang-Yi Fan, Clinton D. Allred, and Robert S. Chapkin
Précis: These findings show that p53 deletion in intestinal stem cells will promote colon cancer only if DNA damage and chronic inflammation are also present.

LETTERS TO THE EDITOR

5398 Melphalan, Antimelanoma Immunity, and Inflammation—Letter
Anna Martner, Junko Johansson, Ilan Ben-Shabat, and Roger Olofsson Bagge

5400 Melphalan, Antimelanoma Immunity, and Inflammation—Response
Abhishek D. Garg, Aleksandra M. Dudek-Peric, and Patrizia Agostinis

CORRECTION

5402 Correction: Genetic Regulation of Fate Decisions in Therapeutic T Cells to Enhance Tumor Protection and Memory Formation

5403 Acknowledgment to Reviewers
ABOUT THE COVER

In CD133-positive tumor-propagating cells from glioblastoma, an intact actin cytoskeleton is required for elevated PLK1 activity, which in turn controls mitotic entry and cell polarity. Taken together, the data suggest a Plk1-driven polarity checkpoint, distinguishing CD133-positive tumor-propagating cells from autologous CD133-negative cells. Elevated PLK1 activity protects CD133-positive tumor-propagating cells from BRAF/MAPK inhibition and sensitizes them to Plk1 inhibition. Using immunocytochemistry, it was found that CD133 failed to localize to the membrane and in a polarized fashion in cells treated with actin polymerization inhibitor Latrunculin A. For details, see article by Lerner and colleagues on page 5355.