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    These findings identify Rab7 as a substrate for TBK1 for regulation of innate immune signaling, thereby providing important insight for strategies aimed at manipulating the immune response to enhance therapeutic efficacy in TNBC.

57  Heparanase and Chemotherapy Synergize to Drive Macrophage Activation and Enhance Tumor Growth
    Udayan Bhattacharya, Lilach Gutter-Kapon, Tal Kan, Ilanit Boyango, Uri Barash, Shi-Ming Yang, Jingling Liu, Miriam Gross-Cohen, Ralph D. Sanderson, Yuval Shaked, Neta Ilan, and Israel Vlodavsky
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    Melissa A. Wilson and Kenneth H. Buettow
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## TUMOR BIOLOGY AND IMMUNOLOGY

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Joseph Chen, Badriprasad Ananthanarayanan, Kelsey S. Springer, Kayla J. Wolf, Sharon M. Sheyman, Vivien D. Tran, and Sanjay Kumar

Targeting the actin-binding proteins LIMK1 and LIMK2 significantly diminishes glioblastoma invasion and spread, suggesting the potential value of these proteins as therapeutic targets.

## TRANSLATIONAL SCIENCE

### 79 A Single-Step, High-Dose Selection Scheme Reveals Distinct Mechanisms of Acquired Resistance to Oncogenic Kinase Inhibition in Cancer Cells
Kenneth J. Finn, Scott E. Martin, and Jeff Settleman

Through modeling resistance to MET kinase inhibition in cultured cancer cells using single-step, high-dose selection, these findings highlight that the specific nature of the selection protocol impacts which resistance mechanisms are identified.

See related commentary, p. 25

### 91 Adhesion of T Cells to Endothelial Cells Facilitates Blinatumomab-Associated Neurologic Adverse Events
Matthias Klinger, Gerhard Zugmaier, Virginie Nägele, Maria-Elisabeth Goebeler, Christian Brandl, Matthias Stelljes, Hans Lassmann, Arend von Stackelberg, Ralf C. Bargou, and Peter Kufer

This study proposes T-cell adhesion to endothelial cells as a necessary but insufficient first step for development of blinatumomab-associated neurological adverse events and suggests interfering with adhesion as a mitigation approach.

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## POPULATION AND PREVENTION SCIENCE

### 116 Recreational Physical Activity Is Associated with Reduced Breast Cancer Risk in Adult Women at High Risk for Breast Cancer: A Cohort Study of Women Selected for Familial and Genetic Risk

These findings suggest that physical activity might reduce breast cancer risk by about 20% for women across the risk continuum, including women at higher-than-average risk due to their family history or genetic susceptibility.

See related commentary, p. 23

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ABOUT THE COVER

The LIM kinase isoforms LIMK1 and LIMK2 (LIMK1/2) modulate actin cytoskeletal dynamics and control cell polarization, migration, and invasion. Thus, LIMK1/2 could potentially be targeted to combat glioblastoma infiltration. Structured illumination microscopy allows super resolution imaging of the actin cytoskeleton in glioblastoma cells expressing a nontargeting shRNA (bottom right), LIMK1 shRNA (top), and LIMK2 shRNA (bottom left). Individual knockdown of either isoform does not significantly compromise actin organization relative to control cells, whereas dual knockdown of both isoforms strongly disrupts actin architecture (not shown). For details, see article by Chen and colleagues on page 69.