VEGF and c-Met Blockade Amplify Angiogenesis Inhibition in Pancreatic Islet Cancer
Weon-Kyoo You, Barbara Sennino, Casey W. Williamson, Beverly Falcon, Hiroya Hashizume, Li-Chin Yao, Dana T. Aftab, and Donald M. McDonald

Précis: Cancer cell-targeted therapeutic agents may achieve efficacy in part by also attacking the tumor microenvironment, as illustrated by this study revealing the antiangiogenesis benefits of MET inhibitors in promoting blood vessel regression, in addition to direct effects against tumor cells themselves.

Podoplanin-Positive Fibroblasts Enhance Lung Adenocarcinoma Tumor Formation: Podoplanin in Fibroblast Functions for Tumor Progression
Ayuko Hoshino, Genichiro Ishii, Takashi Ito, Kazuhiro Aoyagi, Yoichi Ohtaki, Kanji Nagai, Hiroki Sasaki, and Atsushi Ochiai

Précis: Findings define a fibroblast cell type in the perivascular tumor microenvironment that creates a specific niche for tumor progression, suggesting new strategies to block tumor invasion and metastasis.

IL-7 Contributes to the Progression of Human T-cell Acute Lymphoblastic Leukemias
Ana Silva, Angelo B.A. Laranjeira, Leila R. Martins, Bruno A. Cardoso, Jocelyne Demengeot, J. Andrés Yunes, Benedict Seddon, and João T. Barata

Précis: Blocking IL-7 may constitute an effective therapeutic strategy to improve treatment of an aggressive form of T-cell leukemia.

Memory Type 2 Helper T Cells Induce Long-Lasting Antitumor Immunity by Activating Natural Killer Cells
Masayuki Kitajima, Toshihiro Ito, Damon J. Tumes, Yusuke Endo, Atsushi Onodera, Kahoko Hashimoto, Shinichiro Motohashi, Masakatsu Yamashita, Takashi Nishimura, Steven F. Ziegler, and Toshinori Nakayama

Précis: Cancer immunotherapies that recruit an IL4-dependent class of memory T helper cells that can activate antitumor natural killer cells may achieve more potent and durable clinical outcomes.
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**MOLECULAR AND CELLULAR PATHOBIOLOGY**

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PREVENTION AND EPIDEMIOLOGY

4898
Prediagnostic Serum Levels of Cytokines and Other Immune Markers and Risk of Non-Hodgkin Lymphoma
Mark P. Purdue, Qing Lan, Rachel Bagni, William C. Hocking, Dalsu Baris, Douglas J. Reding, and Nathaniel Rothman

Précis: This prospective study identifies elevations in serologic markers associated with future risk of non-Hodgkin lymphoma.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

4908
SPARC Stimulates Neuronal Differentiation of Medulloblastoma Cells via the Notch1/STAT3 Pathway
Praveen Bhoopathi, Chandramu Chetty, Ranadheer Dontula, Meena Gujrati, Dzung H. Dinh, Jasti S. Rao, and Sajani S. Lakka

Précis: This study suggests a differentiation-inducing strategy to increase therapeutic responses in a commonly deadly form of pediatric brain cancer.

4920
Insights into ALK-Driven Cancers Revealed through Development of Novel ALK Tyrosine Kinase Inhibitors
Christine M. Lovly, Johannes M. Heuckmann, Elisa de Stanchina, Heidi Chen, Roman K. Thomas, Chris Liang, and William Pao

Précis: Acquired resistance arising in ALK-fusion positive cancers to a first generation ALK tyrosine kinase inhibitor in clinical trials might be addressed by a novel, more potent, and specific second generation inhibitor.

4932
Caveolin-1 Upregulation Mediates Suppression of Primary Breast Tumor Growth and Brain Metastases by Stat3 Inhibition
Wen-Tai Chiu, Hsueh-Te Lee, Feng-Ju Huang, Kenneth D. Aldape, Jun Yao, Patricia S. Steeg, Cheng-Yang Chou, Zhihmin Lu, Keping Xie, and Suyun Huang

Précis: The mediator of brain metastasis identified in this study is likely a core modifier node of many cancer signaling pathways, since it functions in controlling the formation of plasma membrane lipid rafts that organize many cell surface adhesion and signaling complexes.

4944
Poly(ADP-Ribose) Polymerase Inhibition Synergizes with 5-Fluorodeoxyuridine but not 5-Fluorouracil in Ovarian Cancer Cells
Amelia M. Huehls, Jill M. Wagner, Catherine J. Hunttoon, Liyi Geng, Charles Erlichman, Anand G. Patel, Scott H. Kaufmann, and Larry M. Karnitz

Précis: An analysis of the checkpoint and DNA repair pathway responses activated by floxuridine reveals how to combine these existing chemotherapeutic agents with PARP inhibitors to achieve the best therapeutic efficacy.

4955
Sorafenib Enhances Pemetrexed Cytotoxicity through an Autophagy-Dependent Mechanism in Cancer Cells

Précis: This study defines a novel combination of clinically approved drugs that may prove to be highly effective in the treatment of many types of solid tumors, prompting immediate clinical attention.

4968
Effect of ON 01910.Na, an Anticancer Mitotic Inhibitor, on Cell-Cycle Progression Correlates with RanGAP1 Hyperphosphorylation
Irina A. Oussenko, James F. Holland, E. Premkumar Reddy, and Takao Ohnuma

Précis: This drug mechanism study offers evidence of a new therapeutic pathway that can achieve pathobiological selectivity for cancer cells.

4977
Small-Molecule Anticancer Compounds Selectively Target the Hemopexin Domain of Matrix Metalloproteinase-9
Antoine Dufour, Nicole S. Samson, Jian Li, Cem Kuscu, Robert C. Rizzo, Jennifer L. DeLeon, Jizu Zhi, Nadia Jaber, Eric Liu, Stanley Zucker, and Jian Cao

Précis: Although early MMP inhibitors moved into clinical development were not successful, the central importance of MMPs in cancer invasion and metastasis has driven the development of later generation inhibitors that offer considerable therapeutic potential.
Positive Feedback Loop Between PI3K-Akt-mTORC1 Signaling and the Lipogenic Pathway Boosts Akt Signaling: Induction of the Lipogenic Pathway by a Melanoma Antigen
Yoshio Yamauchi, Keiko Furukawa, Kazunori Hamamura, and Koichi Furukawa

**Précis:** This study suggests a mechanistic explanation for why cancer cells synthesize high levels of cholesterol and fatty acids, which by promoting formation of plasma membrane lipid rafts can reinforce signaling events that sustain cancer cell survival.

**LETTERS TO THE EDITOR**

Myeloid Suppressor Cells Regulate the Lung Environment—**Letter**
Momir Bosiljcic, Melissa J. Hamilton, Judit P. Banath, Nancy E. LePard, Denise C. McDougal, Jessica X. Jia, Gerald Krystal, and Kevin L. Bennewith

Myeloid Suppressor Cells Regulate the Lung Environment—**Response**
Hannah H. Yan, Michael Pickup, Yanli Pang, Agnieszka E. Gorska, Zhaoyang Li, Anna Chyttil, Yipeng Geng, Jerome W. Gray, Harold L. Moses, and Li Yang

**CORRECTION**

Correction: Hsp27 Promotes Insulin-Like Growth Factor-I Survival Signaling in Prostate Cancer via p90Rsk-Dependent Phosphorylation and Inactivation of BAD

**See page 5054**
ABOUT THE COVER

Tumor antigen-reactive CTLs by programming iPS cells infiltrated into tumor tissue. Tumor antigen TCR gene-transduced iPS cells were adoptively transferred into C57BL/6 mice, which were subjected to challenge with E.G7 tumor cells. On day 35 after tumor challenge, tumor tissues were examined for tumor-reactive T-cell infiltration by immunohistological staining. Tumor antigen-specific CTLs (red) infiltrated into lymphoma tissue (green). For details, see the article by Lei and colleagues on page 4742 of this issue.