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**Cancer Research**

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IRF8 Regulates Acid Ceramidase Expression to Mediate Apoptosis and Suppresses Myelogeneous Leukemia
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Précis: Findings define how a critical tumor suppressor gene becomes attenuated in chronic myeloid leukemia, and how this attenuation leads to apoptotic resistance and disease progression.

CD73-Deficient Mice Have Increased Antitumor Immunity and Are Resistant to Experimental Metastasis
John Stagg, Upulie Divisekera, Helene Duret, Tim Sparwasser, Michele W.L. Teng, Phillip K. Darcy, and Mark J. Smyth

Précis: Findings offer preclinical proof-of-concept for therapeutic targeting of a important cell surface-based driver of immune escape in cancer, perhaps involved in many types of human cancer.

FLT3-Mediated p38–MAPK Activation Participates in the Control of Megakaryopoiesis in Primary Myelofibrosis

Précis: Findings advance understanding of the pathophysiology of primary myelofibrosis, a bone marrow–derived disease, and suggest applications for drugs that target a key megakaryocytic signaling pathway as a new strategy to evaluate for treating this disease.

DLC1 Interaction with S100A10 Mediates Inhibition of In Vitro Cell Invasion and Tumorigenicity of Lung Cancer Cells through a RhoGAP-Independent Mechanism
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Précis: Findings reveal a mechanism through which plasminogen activator-dependent conversion of plasminogen to plasmin is attenuated, reducing tumor cell capacity for invasion and metastasis in the tumor microenvironment.

MicroRNA-301 Mediates Proliferation and Invasion in Human Breast Cancer
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The Neuronal Differentiation Factor NeuroD1 Downregulates the Neuronal Repellent Factor Slit2 Expression and Promotes Cell Motility and Tumor Formation of Neuroblastoma

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Précis: Findings establish the critical role of a neuronal differentiation factor in neuroblastoma and its functional relationship with a neuronal repellent factor.

Overexpression of a Novel Activator of PAK4, the CDK5 Kinase–Associated Protein CDK5RAP3, Promotes Hepatocellular Carcinoma Metastasis

Grace Wing-Yan Mak, Mandy Man-Lok Chan, Veronica Yee-Law Leong, Joyce Man-Fong Lee, Tai-On Yau, Irene Oi-Lin Ng, and Yick-Pang Ching

Précis: A gene implicated in cancer progression proves to directly support metastasis by activating a PAK kinase implicated in invasive cell motility.

Functional Cooperation of RKTG with p53 in Tumorigenesis and Epithelial–Mesenchymal Transition

Yuhui Jiang, Xiaoduo Xie, Zhiqiang Li, Zheng Wang, Yixuan Zhang, Zhiqiang Ling, Yi Pan, Zhenzhen Wang, and Yan Chen

Précis: A novel tumor suppressor collaborates with p53 in tumor formation and epithelial-mesenchymal transition.

Cytoplasmic CUL9/PARC Ubiquitin Ligase Is a Tumor Suppressor and Promotes p53-Dependent Apoptosis

Xin-Hai Pei, Feng Bai, Zhijun Li, Matthew D. Smith, Gabrielle Whitewolf, Ran Jin, and Yue Xiong

Précis: This study identifies a potential p53 activating E3 ligase located in the cytoplasm that functions as a tumor suppressor.

Frequent Truncating Mutation of TFAM Induces Mitochondrial DNA Depletion and Apoptotic Resistance in Microsatellite-Unstable Colorectal Cancer


Précis: A class of mutations that lead to mitochondrial DNA depletion and apoptotic resistance may be important drivers of tumorigenesis in most microsatellite-unstable colorectal cancers.

Genome-Wide DNA Methylation Profiling of CpG Islands in Breast Cancer Identifies Novel Genes Associated with Tumorigenicity

Victoria K. Hill, Christopher Ricketts, Ivan Bieche, Sophie Vacher, Dean Gentle, Cheryl Lewis, Eamonn R. Maher, and Farida Latif

Précis: A genome-wide study of DNA methylation patterns suggests clinically useful theranostic markers in breast cancer, as well as new candidate pathways in etiology, progression, and therapy.
High Plasma Levels and Effective Lymphatic Uptake of Docetaxel in an Orally Available Nanotransporter Formulation
Taher Nassar, Suha Attili-Qadri, Oshrat Harush-Frenkel, Shimon Farber, Shimon Lecht, Philip Lazarovici, and Simon Benita

Precise: An oral nanocarrier of docetaxel favors lymphatic uptake in preclinical studies, potentially stimulating clinical studies that could allow docetaxel chemotherapy to be switched from intravenous to oral delivery in patients.

Sildenafil Reverses ABCB1- and ABCG2-Mediated Chemotherapeutic Drug Resistance
Zhi Shi, Amit K. Tiwari, Suneet Shukla, Robert W. Robey, Satyakam Singh, In-Wha Kim, Susan E. Bates, Xingxiang Peng, Ioana Abraham, Suresh V. Ambudkar, Tanaji T. Talele, Li-Wu Fu, and Zhe-Sheng Chen

Precise: A drug used widely to treat erectile dysfunction in men is found to abrogate two common mechanisms of chemotherapeutic drug resistance, with immediate potential applications to improve the treatment of many advanced cancers.

Inhibition of NEDD8-Activating Enzyme Induces Rereplication and Apoptosis in Human Tumor Cells Consistent with Deregulating CDT1 Turnover
Michael A. Milhollen, Usha Narayanan, Teresa A. Soucy, Petter O. Veiby, Peter G. Smith, and Benjamin Amidon

Precise: DNA re-replication elicited in cancer cells by a small molecule inhibitor currently in Phase I trials creates an unrecoverable cellular insult, with implications for gaining deeper understanding of a unique therapeutic mechanism of cytotoxicity in cancer treatment.

PDK1 Attenuation Fails to Prevent Tumor Formation in PTEN-Deficient Transgenic Mouse Models

Precise: This study employed a novel RNAi approach useful for context-dependent target validation in vivo, applying it to demonstrate that the protein kinase PDK1 is not a rate limiting factor for PI3K-pathway activation or tumor formation in PTEN-deficient mouse models.

Frizzled 4 Regulates Stemness and Invasiveness of Migrating Glioma Cells Established by Serial Intracranial Transplantation

Precise: Findings define an important role in glioma recurrence and poor prognosis for a G-protein coupled receptor that is part of the Wnt signaling family governing stemness and invasiveness of glioma stem cells.

FOXQ1 Regulates Epithelial-Mesenchymal Transition in Human Cancers
Yuanyuan Qiao, Xia Jiang, Shuet Theng Lee, R.K. Murthy Karuturi, Shing Chuan Hooi, and Qiang Yu

Precise: Findings identify a member of the FOXO family of transcription factors as a critical regulator of EMT, stem cell properties, and chemotherapeutic resistance in cancer cells.
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Evasion from immune recognition contributes to tumor growth. Stagg and colleagues have recently identified CD73 expression on tumor cells as an important mechanism of tumor immune evasion. The cover image represents CD73 expression (green) detected by immunofluorescence on MDA-MB-231 breast cancer cells. Stagg and colleagues describe that CD73 expression on hematopoietic and nonhematopoietic host cells also contributes to tumor immune evasion. Using adoptive reconstitution of T regulatory cells (Treg), their study defines CD73 as an important immunosuppressive factor expressed by Treg that promotes tumor growth. Their study also reveals that nonhematopoietic expression of CD73, possibly on endothelial cells, enhances metastasis of circulating tumor cells. Finally, they report that anti-CD73 therapy inhibits the growth and metastatic potential of CD73-negative tumor cells. Taken together, their study suggests that CD73 may be targeted at multiple levels to induce anticancer effects. For details, see the article by Stagg and colleagues on page 2892 of this issue.