Précis: Pancreatic cancer is deadly in part because it is so commonly diagnosed late in development due to the lack of symptoms or diagnostic tools that could identify it at earlier stages when it could be managed more effectively.

2491

**Real-time Raman Spectroscopy for In Vivo Skin Cancer Diagnosis**

Harvey Lui, Jianhua Zhao, David McLean, and Haishan Zeng

Précis: A rapid, noninvasive technology with potential for adoption at the clinical point of care is described for ready and accurate diagnosis of skin lesions.

**MICROENVIRONMENT AND IMMUNOLOGY**

**Cyclophosphamide Creates a Receptive Microenvironment for Prostate Cancer Skeletal Metastasis**

Serk In Park, Jinhui Liao, Janice E. Berry, Xin Li, Amy J. Koh, Megan E. Michalski, Matthew R. Eber, Fabiana A. Sok, David Sadler, Sudha Sud, Sandra Tisdelle, Stephanie D. Daignault, Jeffrey A. Nemeth, Linda A. Snyder, Thomas J. Wronsik, Kenneth J. Pienta, and Laurie K. McCauley

Précis: The chemotherapeutic drug cyclophosphamide, used in the treatment of many kinds of cancer, is found unexpectedly to exert a prometastatic effect within bone.
**MOLECULAR AND CELLULAR PATHOBIOLOGY**

### Mitochondrial Bcl-2 Family Dynamics

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<td>Hepatocyte–Stellate Cell Cross-Talk in the Liver Engenders a Permissive Inflammatory Microenvironment That Drives Progression in Hepatocellular Carcinoma</td>
<td>Cédric Coulouarn, Anne Corlu, Denise Glaise, Isabelle Guénon, Snorri S. Thorsteinsson, and Bruno Clément</td>
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<td>2589</td>
<td>Loss of Cell-Surface Laminin Anchoring Promotes Tumor Growth and Is Associated with Poor Clinical Outcomes</td>
<td>Armin Akhavan, Obi L. Griffith, Liliana Soroceanu, Dmitri Leonoudakis, Maria Gloria Luciani-Torres, Anneleen Daemen, Joe W. Gray, and John L. Mischler</td>
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### Parkin Pathway Activation Mitigates Glioma Cell Proliferation and Predicts Patient Survival

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<td>Interleukin-17 Promotes Formation and Growth of Prostate Adenocarcinoma in Mouse Models</td>
<td>Quyang Zhang, Sen Liu, Dongxia Ge, Qingsong Zhang, Yun Xue, Zhenggang Xiong, Asim B. Abdel-Mageed, Leann Myers, Steven M. Hill, Brian G. Rowan, Oliver Sartor, Jonathan Melamed, Zhenbang Chen, and Zongbing You</td>
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### KRas Induces a Src/PEAK1/ErbB2 Kinase Amplification Loop That Drives Metastatic Growth and Therapy Resistance in Pancreatic Cancer

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<td>Dinitroazetidines Are a Novel Class of Anticancer Agents and Hypoxia-Activated Radiation Sensitizers Developed from Highly Energetic Materials</td>
<td>Shoucheng Ning, Mark Bednarski, Bryan Oronsky, Jan Scicinski, Gordon Saul, and Susan J. Knox</td>
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### Mitochondrial Bcl-2 Family Dynamics Define Therapy Response and Resistance in Neuroblastoma

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<td>Coxsackievirus B3 Is an Oncolytic Virus with Immunostimulatory Properties That Is Active against Lung Adenocarcinoma</td>
<td>Shohei Miyamoto, Hiroyuki Inoue, Takahumi Nakamura, Meiko Yamada, Chika Sakamoto, Yasuo Urata, Toshihiko Okazaki, Tomotoshi Marumoto, Atsushi Takahashi, Koichi Takayama, Yoichi Nakanishi, Hiroyuki Shimizu, and Kenzaburo Tani</td>
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**Cancer Research**

*American Association for Cancer Research*
Activation of Ras/Pi3k/ERK Pathway Induces c-Myc Stabilization to Upregulate Argininosuccinate Synthetase, Leading to Arginase Resistance in Melanoma Cells

Wen-Bin Tsai, Isamu Aiba, Yan Long, Hui-Kuan Lin, Lynn Feun, Niramol Savaraj, and Macus Tien Kuo

Precis: Findings offer mechanistic insight into how resistance emerges to arginine deprivation therapy and how inhibitors of the Ras/ERK and PI3K/AKT pathways might restore therapeutic responses.

Mitochondria-Targeted Drugs Synergize with 2-Deoxyglucose to Trigger Breast Cancer Cell Death

Gang Cheng, Jacek Zielonka, Brian P. Dranka, Donna McAllister, A. Craig Mackinnon Jr, Joy Joseph, and Balaraman Kalyanaraman

Precis: This important study may crack the long-standing challenge of how to employ the glycolytic inhibitor 2-deoxyglucose for generalized anticancer therapy, by combining it with mitochondria-targeted cationic compounds that can improve cancer cell cytotoxicity without toxic liabilities to normal tissue.

Smac Mimetic LBW242 Sensitizes XIAP-Overexpressing Neuroblastoma Cells for TNF-α-Independent Apoptosis

Georg Eschenburg, Angelika Eggert, Alexander Schramm, Holger N. Losel, and Patrick Hundsdorfer

Precis: Smac mimetics offer a potential adjuvant approach to sensitize or re sensitize tumors to chemotherapy, as illustrated by this preclinical proof-of-concept study in a commonly deadly type of pediatric cancer.

Epidermal Growth Factor Receptor Variant III Contributes to Cancer Stem Cell Phenotypes in Invasive Breast Carcinoma

Catherine A. Del Vecchio, Kristin C. Jensen, Ryan T. Nitta, A. Hunter Shain, Craig P. Giacomini, and Albert J. Wong

Precis: By identifying breast cancer stem cells that express a variant EGFR receptor, this study has implications for how to improve treatment for patients who harbor this variant receptor.

HER3 is Required for HER2-Induced Preneoplastic Changes to the Breast Epithelium and Tumor Formation

David B. Vaugh, Jamie C. Stanford, Christian Young, Donna J. Hicks, Frank Wheeler, Cammie Rinehart, Violeta Sánchez, John Kolanid, William J. Muller, Carlos L. Arteaga, and Rebecca S. Cook

Precis: Findings offer a preclinical proof-of-concept for a new strategy to treat or prevent HER2-amplified breast cancers, which represent nearly 30% of all breast cancers, by targeting an important heterodimeric partner of HER2.

Real-Time Monitoring of Rare Circulating Hepatocellular Carcinoma Cells in an Orthotopic Model by In Vivo Flow Cytometry Assesses Resection on Metastasis

Zhi-Chao Fan, Jun Yan, Guang-Da Liu, Xiao-Ying Tan, Xiao-Fu Weng, Wei-Zhong Wu, Jian Zhou, and Xun-Bin Wei

Precis: In vivo flow cytometry may offer a breakthrough technology to elucidate mechanisms of hematogenous metastasis and to monitor the efficacy of cancer therapy.

ABOUT THE COVER

Interleukin-17 (IL-17) is a key proinflammatory cytokine involved in many inflammatory and autoimmune diseases. Mice with conditional knockout of PTEN tumor suppressor gene developed invasive prostate adenocarcinomas at ages of 9 to 30 weeks. When IL-17 signaling was blocked by knockout IL-17 receptor C (IL-17RC) in the PTEN-null mice, the number and size of prostate tumors were reduced compared to mice that expressed IL-17RC, because IL-17RC knockout reduced cellular proliferation, increased apoptosis, inhibited inflammatory infiltration, and diminished expression of matrix metalloproteinase 7 in the mouse prostates. For details, see article by Zhang and colleagues on page 2589 of this issue.