# CANCER RESEARCH

## TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Page</th>
<th>Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>2423</td>
<td>BREAKING INSIGHTS</td>
</tr>
<tr>
<td>2425</td>
<td>OBITUARY</td>
</tr>
<tr>
<td>2427</td>
<td>REVIEW</td>
</tr>
<tr>
<td>2437</td>
<td>CANCER RESEARCH HIGHLIGHTS</td>
</tr>
<tr>
<td>2441</td>
<td>GENOME AND EPIGENOME</td>
</tr>
<tr>
<td>2451</td>
<td>MOLECULAR CELL BIOLOGY</td>
</tr>
</tbody>
</table>

### BREAKING INSIGHTS

**2423** Highlights from Recent Cancer Literature

### OBITUARY

**2425** Raymond L. Erikson, PhD: In Memoriam (1936–2020)

### REVIEW

**2427** Shaping Chromatin States in Prostate Cancer by Pioneer Transcription Factors

### CANCER RESEARCH HIGHLIGHTS

**2437** SKP2 My Lou, My Darling

**2439** TAp63–miRNA–AURKA Axis as a Therapeutic Target for Cutaneous Squamous Cell Carcinoma

### GENOME AND EPIGENOME

**2441** Activation of a Subset of Evolutionarily Young Transposable Elements and Innate Immunity Are Linked to Clinical Responses to 5-Azacytidine

**2451** A Genome-Wide Association Study Identifies Two Novel Susceptible Regions for Squamous Cell Carcinoma of the Head and Neck

Sanjay Shete, Hongliang Liu, Jian Wang, Robert Yu, Erich M. Sturgis, Guojun Li, Kristina R. Dahlstrom, Zhensheng Liu, Christopher I. Amos, and Qingyi Wei

Two novel risk loci for SCCHN in non-Hispanic white individuals highlight the importance of immunologic mechanism in the disease etiology.

### MOLECULAR CELL BIOLOGY

**2461** Rb and p53-Deficient Myxofibrosarcoma and Undifferentiated Pleomorphic Sarcoma Require Skp2 for Survival

George Z. Li, Tomoyo Okada, Young-Mi Kim, Narasimhan P. Agaram, Francisco Sanchez-Vega, Yawei Shen, Norifumi Tsubokawa, Jordan Rios, Axel S. Martin, Mark A. Dickson, Li-Xuan Qin, Nicholas D. Socci, and Samuel Singer

Loss of both Rb and p53 renders myxofibrosarcoma and undifferentiated pleomorphic sarcoma dependent on Skp2, which could provide the basis for promising novel systemic therapies.

**2472** MAFB Promotes Cancer Stemness and Tumorigenesis in Osteosarcoma through a Sox9-Mediated Positive Feedback Loop

Yanyan Chen, Tao Wang, Mengxi Huang, Qin Liu, Chao Hu, Bin Wang, Dong Han, Cheng Chen, Jundiang Zhang, Zhiping Li, Chao Liu, Wenbin Lei, Yue Chang, Meijuan Wu, Dan Xiang, Yitian Chen, Rui Wang, Weiqian Huang, Zhengle Li, and Xiaoyuan Chu

Transcription factors MAFB and Sox9 form a positive feedback loop to maintain cell stemness and tumor growth in vitro and in vivo, revealing a potential target pathway for therapeutic intervention in osteosarcoma.
Induction of DNMT3B by PGE2 and IL6 at Distant Metastatic Sites Promotes Epigenetic Modification and Breast Cancer Colonization

Jae Young So, Nicolas Skrypek, Howard H. Yang, Anand S. Merchant, George W. Nelson, Wei-Dong Chen, Hiroki Ishii, Jennifer M. Chen, Gangqing Hu, Bhagelu R. Achyut, Esther C. Yoon, Liying Han, Chuanshu Huang, Margaret C. Cam, Keji Zhao, Maxwell P. Lee, and Li Yang

These findings reveal that DNMT3B epigenetically regulates multiple pro-oncogenic signaling pathways via the inflammatory microenvironment at distant sites, cautioning the clinical approach basing current therapies on genetic characterization of primary tumors.

Myeloid Cell–Derived TGFβ Signaling Regulates ECM Deposition in Mammary Carcinoma via Adenosine-Dependent Mechanisms

Georgii Vasiukov, Tatiana Novitskaya, Andries Zijlstra, Philip Owens, Fei Ye, Zhuo Zhao, Harold L. Moses, Timothy Blackwell, Igor Feoktistov, and Sergey V. Novitskiy

TGFβ signaling on fibroblasts is decreased in breast cancer, correlates with poor prognosis, and appears to be driven by adenosine that accelerates tumor progression and metastasis via ECM remodeling.

Blocking Angiopoietin-2 Promotes Vascular Damage and Growth Inhibition in Mouse Tumors Treated with Small Doses of Radiation

Pauliina Kallio, Elina Jokinen, Jenny Höögström, Suvendu Das, Sarika Heino, Marianne Låhde, Jefim Brodkin, Emilia A. Korhonen, and Kari Alitalo

These findings offer a preclinical rationale for further testing of the use of radiation in combination with Ang2-blocking antibodies to improve the overall outcome of cancer treatment.

Secretion of Acid Sphingomyelinase and Ceramide by Endothelial Cells Contributes to Radiation-Induced Intestinal Toxicity

Daniela Leonetti, Hala Estéphan, Natacha Ripoche, Nolwenn Dubois, Audrey Aguesse, Sébastien Gouraud, Lisa Brossard, Sophie Chiavassa, Isabelle Corre, Claire Pecqueur, Michel Neunlist, Elie Hadchity, Marie-Hélène Gaugler, Maxime M. Mahé, and François Paris

This study identifies secreted ASM and ceramide as paracrine factors enhancing intestinal epithelial dysfunction, revealing a previously unknown class of mediators of radiosensitivity.

Telomere Maintenance Mechanisms Define Clinical Outcome in High-Risk Neuroblastoma


These findings assess telomere maintenance mechanisms with TERT mRNA and the ALT DNA biomarker C-circles to stratify neuroblastoma into three groups, with distinct overall survival independent of currently used clinical risk classifiers.
ABOUT THE COVER

Shown are three-dimensional (3D) mouse enteroid-derived C57Bl/6 mouse crypts after Hoechst staining under observation by confocal microscopy. Enteroids are small intestine organoids containing fully differentiated and polarized epithelium with a central lumen. This novel 3D culture model allows deeper investigation of small intestine radiotoxicity, which is a common side effect of abdominal radiation therapy. The use of enteroids culture reveals how the sphingolipid ceramide and its hydrolysis enzyme, the acid sphingomyelinase secreted by irradiated endothelial cells, are modulating size, shape, and number of enteroids after radiation. For details, see article by Leonetti and colleagues on page 2651.