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*Cancer Research* is a weekly journal that publishes original research in all areas of cancer biology and medicine. It covers a wide range of topics from basic research to clinical applications, providing a comprehensive overview of the latest developments in the field of cancer research. The journal is published by the American Association for Cancer Research (AACR) and is one of the most respected journals in the field of oncology. Each issue contains a variety of sections, including Breaking Advances, Reviews, Priority Reports, Clinical Studies, and Integrated Systems and Technologies, among others. The table of contents provides an overview of the articles featured in the issue, highlighting the latest research findings and developments in cancer biology and medicine.
5999  MYCN-Dependent Expression of Sulfatase-2 Regulates Neuroblastoma Cell Survival
Valeria Solari, Lucia Borriello, Gianluca Turcatel, Hiroyuki Shimada, Richard Spoto,
G. Esteban Fernandez, Shahab Asgharzadeh, Edwin A. Yates, Jeremy E. Turnbull, and
Yves A. DeClerck
Précis: An enzyme responsible for modifying extracellular proteoglycans appears to be an important mediator of the effects of the MYCN oncogene in a deadly pediatric tumor, offering new insights into how MYCN drives malignancy by altering the tumor microenvironment.

6010  Vaccine-Elicited CD8⁺ T Cells Cure Mesothelioma by Overcoming Tumor-Induced Immunosuppressive Environment
Zhiwu Tan, Jingying Zhou, Allen K.L. Cheung, Zhe Yu, Ka-Wai Cheung, Jianguo Liang,
Haibo Wang, Boon Kiat Lee, Kwan Man, Li Liu, Kwok-Yung Yuen, and Zhiwei Chen
Précis: DNA vaccination can achieve complete cure of mesothelioma by eliciting enhanced CD8⁺ T cells that can overcome the tumor-induced immunosuppressive environment.

6022  Adverse Immunoregulatory Effects of 5FU and CPT11 Chemotherapy on Myeloid-Derived Suppressor Cells and Colorectal Cancer Outcomes
Julia Kanterman, Moshe Sade-Feldman, Moshe Biton, Elinar Ish-Shalom, Audrey Lasry,
Aviya Goldshtein, Ayala Hubert, and Michal Baniyash
Précis: FOLFIRI, a combination chemotherapy regimen used widely in patients with gastrointestinal cancers, may reinforce immunosuppression and thereby limits the benefits to be gained by recruiting the immune system to improve patient treatment.

6048  Reducing CD73 Expression by IL1β-Programmed Th17 Cells Improves Immunotherapeutic Control of Tumors
Shilpak Chatterjee, Krishnamurthy Thyagarajan, Pravin Kesarwani, Jin H. Song,
Myroslawa Soloshchenko, Jianing Fu, Stefanie R. Bailey, Chenthamarkshan Vasu,
Andrew S. Kraft, Chrystal M. Paulos, Xue-Zhong Yu, and Shikhar Mehrotra
Précis: These findings show that including TGFβ in ex vivo cultures used to program Th17 cells damages their immunotherapeutic potential, and they show how this potential can be more potently realized for adoptive T-cell immunotherapy in cancer patients.

6060  IPH4102, a Humanized KIR3DL2 Antibody with Potent Activity against Cutaneous T-cell Lymphoma
Anne Marie-Cardine, Nicolas Vialaud, Nicolas Thonnart, Rachel Joly, Stéphanie Chanteux,
Laurent Gauthier, Cécile Bonnafous, Benjamin Rossi, Mathieu Bléry, Carine Paturel,
Armand Bensussan, Martine Bagot, and Hélène Sicard
Précis: This study offers a preclinical proof of concept for development of a novel therapy that targets one of the most relevant tumor antigens in cutaneous T-cell lymphoma, where there remains unmet medical need.

6071  Whole-Genome Sequencing of Asian Lung Cancers: Second-Hand Smoke Unlikely to Be Responsible for Higher Incidence of Lung Cancer among Asian Never-Smokers
Vidhya G. Krishnan, Philip J. Ebert, Jason C. Ting, Elaine Lim, Swee-Seong Wong, Audrey S.M. Teo,
Xing Yu, Hui-Hoon Chua, Xiwen Ma, Gary S.L. Loh, Yu-Jen Lin, Joanna H.J. Tan, Kun Yu,
Shenli Zhang, Christoph Reinhard, Daniel S.W. Tan, Brock A. Peters, Stephen E. Lincoln,
Dennis G. Ballinger, Jason M. Laramie, Geoffrey B. Nilsen, Thomas D. Barber, Patrick Tan,
Axel M. Himmel, and Pauline C. Ng
Précis: This whole genome study of Asian lung cancer patients, the largest performed to date, refutes the long-standing presumption that Asian never-smokers have a higher incidence of lung cancer due to second-hand smoke, which does not appear to be the case.
HTLV-1 bZIP Factor HBZ Promotes Cell Proliferation and Genetic Instability by Activating OncomiRs

6094 ALK-Dependent Control of Hypoxia-Inducible Factors Mediates Tumor Growth and Metastasis

6107 Metastatic Heterogeneity of Breast Cancer Cells Is Associated with Expression of a Heterogeneous TGFβ-Activating miR424–503 Gene Cluster

6119 Stress Response Protein Cirp Links Inflammation and Tumorigenesis in Colitis-Associated Cancer

6129 Molecular Characterization of Chronic-type Adult T-cell Leukemia/Lymphoma

6139 Definition of Smad3 Phosphorylation Events That Affect Malignant and Metastatic Behaviors in Breast Cancer Cells

6150 Pro-Oncogenic Role of Alternative p38 Mitogen-Activated Protein Kinases p38γ and p38δ, Linking Inflammation and Cancer in Colitis-Associated Colon Cancer

6161 BRCA1 Suppresses Epithelial-to-Mesenchymal Transition and Stem Cell Dedifferentiation during Mammary and Tumor Development
A Recurrent Activating \textit{PLCG1} Mutation in Cardiac Angiosarcomas Increases Apoptosis Resistance and Invasiveness of Endothelial Cells

Kristin Kunze, Tilmann Speiker, Ulrike Gamerding, Kerstin Nau, Johannes Berger, Thomas Dreyer, Jurgen R. Sindermann, Andreas Hoefmeier, Stefan Gattenlohner, and Andreas Bauninger

\textbf{Précis:} Mutation of \textit{PLCG1} identified in rare tumor may provide insights into apoptosis resistance and invasion.

Genetic Deletion of AEG-1 Prevents Hepatocarcinogenesis


\textbf{Précis:} This potentially seminal study unravels a novel role for the AEG-1 oncogene in shaping the tumor microenvironment in a manner that is essential for liver cancer development.

Vitamin D Suppresses Leptin Stimulation of Cancer Growth through microRNA

Ravi Kasiappan, Yuefeng Sun, Panida Lungchukiet, Waise Quarni, Xiaohong Zhang, and Wenlong Bai

\textbf{Précis:} This study suggests that vitamin D supplements may help obese women reduce their risk of cancer.

Therapeutic Targeting of \textit{BRCA1}-Mutated Breast Cancers with Agents That Activate DNA Repair

Elizabeth Alli, David Solow-Cordero, Stephanie C. Casey, and James M. Ford

\textbf{Précis:} This work offers a preclinical proof of concept for a wholly new approach to chemoprevention in carriers of \textit{BRCA1} mutations as a strategy to reduce the prevalence of \textit{BRCA1}-associated malignancy.

Pretargeted Dual-Modality Immuno-SPECT and Near-Infrared Fluorescence Imaging for Image-Guided Surgery of Prostate Cancer


\textbf{Précis:} This study describes a major advancement to methods used in surgical resections of primary prostate cancer, where image-guided techniques are increasingly important and can extend time to progression in patients.

Pancreatic Cancer—Specific Cell Death Induced \textit{In Vivo} by Cytoplasmic-Delivered Polyinosine—Polycytidylic Acid

Praveen Bhoopathi, Bridget A. Quinn, Qin Gui, Xue-Ning Shen, Steven R. Grossman, Swadesh K. Das, Devanand Sarkar, Paul B. Fisher, and Luni Emdad

\textbf{Précis:} These findings offer a preclinical proof of concept for immediate evaluation of an immune adjuvant that also triggers apoptosis in pancreatic cancer cells, as a novel type of immunochemotherapy to treat pancreatic cancer.

A Small-Molecule Modulator of the Tumor-Suppressor miR34a Inhibits the Growth of Hepatocellular Carcinoma

Zhangang Xiao, Chi Han Li, Stephen L. Chan, Feiyue Xu, Lu Feng, Yan Wang, Jian-Dong Jiang, Joseph J.Y. Sung, Christopher H.K. Cheng, and Yangchao Chen

\textbf{Précis:} These findings offer preclinical proof of concept for a lead small molecule candidate as a new class of therapeutic for liver cancer, based on restoration of miR-34a tumor suppressor function.
Activated d16HER2 Homodimers and SRC Kinase Mediate Optimal Efficacy for Trastuzumab

Lorenzo Castagnoli, Manuela Iezzi, Gaia C. Ghedini, Valentina Ciravolo, Giulia Marzano, Alessia Lamolinara, Roberta Zappasodi, Patrizia Gasparini, Manuela Campiglio, Augusto Amici, Claudia Chiodoni, Arianna Palladini, Pier Luigi Lollini, Tiziana Triulzi, Sylvie Menard, Patrizia Nanni, Elda Tagliabue, and Serenella M. Pupa

Précis: Mouse genetic and clinical results establish the variant HER2 signaling axis as a marker for optimal responses to trastuzumab treatment, with immediate clinical implications.

Effective Cancer Vaccine Platform Based on Attenuated Salmonella and a Type III Secretion System


Précis: This study describes an orally administered Salmonella-based vector system that can present tumor antigens to the immune system in a manner that yields potent antitumor responses, offering a novel platform for the engineering of more effective cancer vaccines.

Targeted Noninvasive Imaging of EGFR-Expressing Orthotopic Pancreatic Cancer Using Multispectral Optoacoustic Tomography

Shanice V. Hudson, Justin S. Huang, Wenyuan Yin, Sabrin Albeituni, Jamie Rush, Anil Khanal, Jun Yan, Brian P. Corea, Hermann B. Frieboes, and Lacey R. McNally

Précis: The technology described in this report offers the potential to detect pancreatic tumors with higher specificity and sensitivity, in both the preclinical and clinical settings, than existing technology permits.

miR326 Maturation Is Crucial for VEGF-C–Driven Cortactin Expression and Esophageal Cancer Progression

Chih-Chen Hong, Pai-Sheng Chen, Jian Chiu, Ching-Feng Chiu, Ching-Yao Yang, Michael Hsiao, Yi-Wen Chang, Yang-Hao Yu, Mien-Chie Hung, Nai-Wen Hsu, Shine-Gwo Shiah, Nan-Yung Hsu, and Jen-Liang Su

Précis: These findings offer insights into how a key driver of esophageal cancer enhances its robust invasive and metastatic properties, with potential implications for the development of new biomarkers or therapies in this setting.

Distinct Subpopulations of Head and Neck Cancer Cells with Different Levels of Intracellular Reactive Oxygen Species Exhibit Diverse Stemness, Proliferation, and Chemosensitivity

Ching-Wen Chang, Yu-Syuan Chen, Shiu-Huey Chou, Chia-Li Han, Yu-Ju Chen, Cheng-Chieh Yang, Chih-Yang Huang, and Jing-Fan Lo

Précis: These findings suggest that strategies to stimulate low intracellular ROS levels, found here to be associated with stemness and chemoresistance in head and neck squamous cancers, should be explored clinically in combination with conventional chemotherapy.

PAD2 Overexpression in Transgenic Mice Promotes Spontaneous Skin Neoplasia


Précis: These findings provide a mechanistic rationale to target a highly tractable enzyme to prevent or treat inflammation-associated skin carcinomas.

SCCA1/SerpinB3 Promotes Oncogenesis and Epithelial-Mesenchymal Transition via the Unfolded Protein Response and IL6 Signaling

Namratha Sheshadri, Joseph M. Catanzaro, Alex J. Bott, Yu Sun, Erica Ullman, Emily I. Chen, Ji-An Pan, Song Wu, Howard C. Crawford, Jianhua Zhang, and Wei-Xing Zong

Précis: A protease inhibitor that is overexpressed in many human cancers is found to promote tumorigenesis by upregulating IL6 signaling in the tumor microenvironment.
6330  Transient SNAIL1 Expression Is Necessary for Metastatic Competence in Breast Cancer
Hung D. Tran, Krishna Luitel, Michael Kim, Kun Zhang, Gregory D. Longmore, and David D. Tran

Précis: These findings provide a compelling genetic rationale to target metastasis by impeding a major regulator of this process despite its transient requirement.

6341  Holo-Retinol–Binding Protein and Its Receptor STRA6 Drive Oncogenic Transformation
Daniel C. Berry, Liraz Levi, and Noa Noy

Précis: Results suggest that the blood carrier of vitamin A and its cell surface transporter and signaling receptor STRA6 may comprise novel targets for cancer therapy.

6352  Ceramide Kinase Promotes Tumor Cell Survival and Mammary Tumor Recurrence
Ania W. Payne, Dhruv K. Pant, Tien-Chi Pan, and Lewis A. Chodosh

Précis: Results identify an actionable pathway in breast cancer patients that might be blocked during chemotherapy to limit tumor recurrence and extend survival.

6364  Notch Signaling Drives Stemness and Tumorigenicity of Esophageal Adenocarcinoma
Zhiqiang Wang, Thiago G. Da Silva, Ke Jin, Xiaojing Han, Prathibha Ranganathan, Xiaoxia Zhu, Avencia Sanchez-Mejias, Feng Bai, Bin Li, Dennis Liang Fei, Kelly Weaver, Rodrigo Vasquez-Del Carpio, Anna E. Moscowitz, Vadim P. Koshenkov, Lilly Sanchez, Lynne Sparling, Xin-Hai Pei, Dido Franceschi, Alan S. Livingstone, and Anthony J. Capobianco

Précis: This study provides a preclinical proof of concept for the repositioning of gamma-secretase inhibitors, previously evaluated in clinical trials, as a new treatment for aggressive esophageal cancers.

ABOUT THE COVER

Astrocyte elevated gene-1 (AEG-1) is an oncogene that is overexpressed in all cancers. Although the oncogenic function of AEG-1 has been studied in tumor cells, as yet the role of AEG-1 in tumor microenvironment cells has not been analyzed. Using immunofluorescence it was documented that AEG-1 is expressed at a high level in macrophages, and functional studies documented that macrophage AEG-1 plays an important role in regulating NF-kB activation and thereby initiation of hepatocarcinogenesis. For details, see article by Robertson and colleagues on page 6184.

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