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4629 Tumor Promotion by Intratumoral Plasmacytoid Dendritic Cells Is Reversed by TLR7 Ligand Treatment
Isabelle Le Mercier, Dominique Poujol, Amélie Sanlaville, Vanja Sisirak, Michael Gobert, Isabelle Durand, Bertrand Dubois, Isabelle Treilleux, Jacqueline Marvel, Jaromir Vlach, Jean-Yves Blay, Nathalie Bendriss-Vermare, Christophe Caux, Isabelle Puisieux, and Nadège Goutagny

Précis: This study suggests a new use in breast cancer treatment for synthetic ligands of TLR7 like imiquimod that are used widely as immunomodulators in clinic.

4641 Vaccine-Instructed Intratumoral IFN-γ Enables Regression of Autochthonous Mouse Prostate Cancer in Allogeneic T-Cell Transplantation
Rodrigo Hess Michelini, Teresa Manzo, Tabea Sturmheit, Veronica Basso, Martina Rocchi, Massimo Freschi, Joanna Listopad, Thomas Blankenstein, Matteo Bellone, and Anna Mondino

Précis: Findings argue that cancer vaccines that improve antitumor T-cell responses can cooperate strongly with allogeneic bone marrow transplants to convert them into effective treatments for solid tumors.

4653 IL-18–Primed Helper NK Cells Collaborate with Dendritic Cells to Promote Recruitment of Effector CD8+ T Cells to the Tumor Microenvironment
Jeffrey L. Wong, Erik Berk, Robert P. Edwards, and Pawel Kalinski

Précis: Results advance understanding of how NK cells can provide an initial stimulus to orchestrate the attraction of dendritic cells and additional effector cells into the cancer microenvironment.

4663 Potent Immunomodulatory Effects of the Trifunctional Antibody Catumaxomab
Diane Goëtée, Caroline Flamant, Sylvie Busakiewicz, Vichnou Poirier-Colame, Oliver Kepp, Isabelle Martins, Julien Pesquet, Alexander Eggermont, Dominique Elias, Nathalie Chaput, and Laurence Zitvogel

Précis: This study reports a comprehensive dissection of the immunomodulatory effects of a bispecific mAb specific for a widely expressed tumor cell adhesion molecule and the T-cell molecule CD3, which is one of the first bispecific mAbs to be explored in clinic.
Histone Demethylase RBP2 Promotes Lung Tumorigenesis and Cancer Metastasis
Yu-Ching Teng, Cheng-Feng Lee, Ying-Shiau Li, Yi-Ren Chen, Pei-Wen Hsiiao, Meng-Yu Chan, Meng-Daw Tsai, and Li-Jung Juan

Precise: Findings establish an oncogenic function in lungs for an Rb binding protein that modifies chromatin, with implications for malignant progression in this tissue.
THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

Novel Recombinant Human B7–H4 Antibodies Overcome Tumoral Immune Escape to Potentiate T-Cell Antitumor Responses
Denarda Dangaj, Evripidis Lanitis, AiZhi Zhao, Shree Joshi, Yi Cheng, Raphael Sandaltzopoulos, Hyun-jeong Ra, Gwenn Danet-Desnoyers, Daniel J. Powell, Jr, and Nathalie Scholler
Précis: Blockade of inhibitory T-cell receptor signals in the same general family as the CTLA-4 molecule targeted by ipilimumab (Yervoy) may offer a paradigm for simultaneous targeting of not only tumor cells, but also tumor-associated macrophages that drive immune escape.

Transcription Poisoning by Topoisomerase I Is Controlled by Gene Length, Splice Sites, and miR-142-3p
Stéphanie Solier, Michael C. Ryan, Scott E. Martin, Sudhir Varma, Kurt W. Kohn, Hongfang Liu, Barry R. Zeeberg, and Scott E. Martin
Précis: Camptothecins used in cancer therapy may act to a major extent by targeting a p53-dependent microRNA.

C-RAF Mutations Confer Resistance to RAF Inhibitors
Rajee Antony, Caroline M. Emery, Allison M. Sawyer, and Levi A. Garraway
Précis: These findings may provide a rationale for the future development of allosteric or pan-RAF inhibitors that disrupt the RAF dimerization interface.

Pivotal Role of the Lipid Raft SK3–Orai1 Complex in Human Cancer Migration and Bone Metastases
Précis: This study links a therapeutically targetable potassium channel to bone metastasis, a common feature of advanced breast and prostate cancers that is generally untreatable.

Docetaxel Conjugate Nanoparticles That Target α-Smooth Muscle Actin–Expressing Stromal Cells Suppress Breast Cancer Metastasis
Mami Murakami, Mark J. Ernsting, Elijus Undzys, Nathan Holwell, Warren D. Foltz, and Shyh-Dar Li
Précis: A novel cytotoxic nanoparticle that specifically degrades stromal elements in the tumor microenvironment exhibits potent antitumor activity.

PREVENTION AND EPIDEMIOLOGY

Pathway-Based Serum microRNA Profiling and Survival in Patients with Advanced Stage Non-Small Cell Lung Cancer
Yan Wang, Jian Gu, Jack A. Roth, Michelle A.T. Hildebrandt, Scott M. Lippman, Yuanqing Ye, John D. Minna, and XiFeng Wu
Précis: Accumulating evidence argues that microRNA signatures derived from blood serum may offer simple quantitative tools for clinical prognosis and therapeutic development in many settings.

A 20-Year Prospective Study of Plasma Prolactin as a Risk Marker of Breast Cancer Development
Shelley S. Tworoger, A. Heather Eliassen, Xuehong Zhang, Jing Qian, Patrick M. Slass, Bernard A. Rosner, and Susan E. Hankinson
Précis: Elevated levels of plasma prolactin are associated with an increased risk of breast cancer, but only for 10 years after assessment of this risk marker, supporting a role for prolactin in later stages in breast carcinogenesis.

Genetic Ablation of the Fatty Acid-Binding Protein FABP5 Suppresses HER2-Induced Mammary Tumorigenesis
Liraz Levi, Glenn Lobo, Mary Kathryn Doud, Johannes von Lintig, Darcie Seachrist, Gregory P. Tochtrop, and Noa Noy
Précis: A protein that delivers fatty acids to the transcription factor PPARG3 is critical for mammary tumor development, rationalizing the development of FABP5 inhibitors to prevent or treat breast cancer.

PanIN-Specific Regulation of Wnt Signaling by HIF2α during Early Pancreatic Tumorigenesis
Angela Criscimanna, Li-Juan Duan, Julie A. Rhodes, Volker Fendrich, Emily Wickline, Douglas J. Hartman, Satyadhar P.S. Monga, Michael T. Lotze, George K. Gittes, Guo-Hua Fong, and Farzad Esni
Précis: This study identifies root signaling connections between hypoxia control and the Wnt and Smad4 pathways in early development of pancreatic cancer.

Enhanced Radiation Sensitivity in HPV-Positive Head and Neck Cancer
Précis: Activation of residual p53 in HPV+ head and neck cancers may explain why this type of disease has a relatively better outcome in patients.

Pathway-Based Serum microRNA Enhance Radiation Sensitivity in PanIN-Specific Regulation of Wnt Genetic Ablation of the Fatty Acid-Binding Protein FABP5 Suppresses HER2-Induced Mammary Tumorigenesis
LIN28 Expression in Malignant Germ Cell Tumors Downregulates let-7 and Increases Oncogene Levels

Precis: This study defines a common oncogenic pathway in malignant germ cell tumors (GCT) and offers preclinical initial proof of concept for its targeting potential in this setting.

A Renewable Tissue Resource of Phenotypically Stable, Biologically and Ethnically Diverse, Patient-Derived Human Breast Cancer Xenograft Models
Xiaomei Zhang, Sofie Claerhout, Aleix Pratt, Lacey E. Dobrolecki, Ivana Petrovic, Qing Lai, Melissa D. Landis, Lisa Wiechmann, Lisa Wong, Suzanne W. Fuqua, Alejandra Contreras, Carolina Gutierrez, Jian Huang, Sufeng Mao, Anne C. Pavlick, Amber M. Froehlich, Meng-Fen Wu, Anna Tsimelzon, Susan G. Hilsenbeck, Edward S. Chen, Pavel Zuloaga, Chad A. Shaw, Gordon B. Mills, Jenny C. Chang, and Michael T. Lewis

Precis: This well-characterized collection of human breast cancer xenografts will serve as a foundation for conduct of “animal clinical trials” to evaluate experimental therapeutics, as well as a resource for mechanistic studies of treatment resistance and metastasis.

elf4B Phosphorylation by Pim Kinases Plays a Critical Role in Cellular Transformation by Abl Oncogenes
Jianling Yang, Jun Wang, Ke Chen, Guijie Guo, Runjiao Xi, Paul B. Rothman, Douglas Whitten, Lianfeng Zhang, Shile Huang, and Ji-Long Chen

Precis: Results identify the translation initiation factor elf4B as a critical substrate of Pim kinases, which mediate the activity of Abl oncogenes, suggesting this factor as a candidate therapeutic target in Abl-induced cancers.

Canonical Wnt Signaling Is Required for Pancreatic Carcinogenesis
Yaqing Zhang, John P. Morris IV, Wei Yan, Heather K. Schofield, Austin Gurney, Diane M. Simeone, Sarah E. Millar, Timothy Hoey, Matthias Hebrok, and Marina Pasca di Magliano

Precis: This study establishes a causal role for WNT pathway signaling in the development and progression of K-ras-initiated pancreatic cancers, with therapeutic implications for the use of WNT pathway antagonists in this deadly disease.

Retraction: Sp100 as a Potent Tumor Suppressor: Accelerated Senescence and Rapid Malignant Transformation of Human Fibroblasts through Modulation of an Embryonic Stem Cell Program
Ron C.J. Schackmann, Sjoerd Klarenbeek, Eva J. Vlug, Susan Stelloo, Miranda van Amersfoort, Milou Tenhagen, Tanya M. Braumüller, Jeroen F. Vermeulen, Petra van der Groep, Ton Peeters, Elke van der Wall, Paul J. van Dijck, Jos Jonkers, and Patrick W.B. Derksen

Precis: A factor well studied in the TNF response and implicated in innate and adaptive immune control is established in this study to control tumor angiogenesis.

TRAF6 Upregulates Expression of HIF-1α and Promotes Tumor Angiogenesis
Heng Sun, Xue-Bing Li, Ya Meng, Li Fan, Min Li, and Jing Fang

Precis: Based on conditional mouse models of metastatic breast cancer that are immunocompetent and clinically relevant, the current study provides an alternate rationale for therapeutic intervention of p120-catenin negative invasive breast cancer.

Correction: IKK4a/ARF Inactivation with Activation of the NF-κB/IL-6 Pathway Is Sufficient to Drive the Development and Growth of Angiosarcoma
Hariharan Iyer, Nathaniel M. Carneiro, Jelena Popovic, Xinyun Shi, Wanjun Xu, Russell E. Cofield, Jr, and Zhen Zeng

Precis: Inactivation of ARF and activation of the NF-κB/IL-6 pathway is sufficient to drive the development and growth of angiosarcoma.
ABOUT THE COVER

Schematic representation of the IRE1α-dependent activation loop that controls tumor cell adaptation. Tumor cell is presented in light gray, stromal cells in dark gray. Proteins are represented by circles, with upregulation in green and downregulation in red. Connections following stress-mediated activation of IRE1α are presented in green for activation and red for inhibition. For details, see article by Pluquet and colleagues on page 4732.