Cancer Research
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Norbert W. Lutz, Yann Le Fur, Johanna Chiche, Jacques Pouysségur, and Patrick J. Cozzone

PRÉCIS: By providing important details on cancer acidity, pH calculations could help support the development of new cancer therapeutics targeting tumor metabolism.

4631 Potent Immunomodulatory Effects of the Trifunctional Antibody Catumaxomab
Diane Goër, Caroline Flamant, Sylvie Busakiewicz, Vichnou Puoirier-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.

MICROENVIRONMENT AND IMMUNOLOGY
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 Sturmhein, Veronica Basso, Martina Rocchi, Massimo Freschi, Joanna Listopad, Thomas Blankenstein, Matteo Bollone, 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 Potential Immunotherapeutic Applications of the Bispecific Antibody BCMAxCD3
Markus R. Grabbe, Ying De, Richard Kuroda, Wei Cao, Tyler F. Norris, Robin A. Amin, Yi Tan, Aljoscha P. Schmalfeldt, Siew-Yen Yew, Robert A. Gross, Michael E. Curiel, and Jere N. Andreff

PRÉCIS: This study reports a comprehensive dissection of the immunotherapeutic potential 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-Shiuan Li, Yi-Ren Chen, Pei-Wen Hsiao, Meng-Yu Chan, Ming-Daw Tsai, and Li-Jung Juan

Précis: Findings establish an oncogenic function in lungs for an Rb binding protein that modifies chromatin, with implications for malignant progression in this tissue.

Intravital FLIM-FRET Imaging Reveals Dasatinib-Induced Spatial Control of Src in Pancreatic Cancer


Précis: Defining the spatial and temporal factors that limit drug targeting in live tumors could help optimize the preclinical development of new therapeutic agents.

PLZF Confers Effector Functions to Donor T Cells That Preserve Graft-versus-Tumor Effects while Attenuating GVHD

Arnab Ghosh, Amanda M. Holland, Yildirim Dogan, Nury L. Yim, Ulltarn K. Rao, Lauren E. Young, Mallory L. West, Natalie V. Singer, Hae Lee, Il-Kang Na, Jennifer J. Tsai, Robert R. Feng, Olaf Penack, Alan M. Hanash, Cecilia Lezcano, George F. Murphy, Chen Liu, Michel Sadelain, Martin G. Sauer, Derek San’tAngelo, and Marcel R.M. van den Brink

Précis: This study describes a strategy to improve the qualities of adoptive cell therapies that use alloreactive T cells for immune treatment of cancer, focusing particularly on the reduction of undesirable graft-versus-host side effects.

Progestrone Receptor Signaling in the Microenvironment of Endometrial Cancer Influences Its Response to Hormonal Therapy

Deanna M. Janzen, Miguel A. Rosales, Daniel Y. Paik, Daniel S. Lee, Daniel A. Smith, Owen N. Witte, M. Luisa Iruela-Arispe, and Sanaz Memarzadeh

Précis: Striking findings show that the efficacy of hormonal therapy in endometrial cancer is not related to effects on cancer cells, but rather to effects on stromal cells where the progesterone receptor is necessary and sufficient to mediate antitumor effects in the microenvironment.

Proteomic and Lipidomic Signatures of Lipid Metabolism in NASH-Associated Hepatocellular Carcinoma

Kyle Muir, Antonious Hazim, Ying He, Marion Peyressatre, Do-Young Kim, Xiaoling Song, and Laura Beretta

Précis: This study reveals a role for lipid-modifying enzymes in liver cancer, identifying in particular a specific type of long-chain polyunsaturated fatty acid participating in nonalcoholic steatohepatitis and liver cancer risk.

Posttranscriptional Regulation of PER1 Underlies the Oncogenic Function of IRE1α


Précis: Circadian rhythms that may affect chemotherapeutic efficacy are linked here for the first time to the unfolded protein response, a signaling pathway widely activated in cancer that plays an important role in tumor aggressiveness.

Peroxiredoxin-2 Represses Melanoma Metastasis by Increasing E-Cadherin/β-Catenin Complexes in Adherens Junctions

Doo Jae Lee, Dong Hoon Kang, Mina Choi, Yang Ji Choi, Joo Young Lee, Joo Hyun Park, Yoon Jung Park, Kyung Wha Lee, and Sang Won Kang

Précis: In discovering a specific antioxidant enzyme that can repress melanoma metastasis, this study also suggests a tractable new direction to treat this deadly disease.

TR3 Modulates Platinum Resistance in Ovarian Cancer

Andrew J. Wilson, Annie Y. Liu, Joseph Roland, Oluwafumilayo A. Adebayo, Sarah A. Fletcher, James C. Slaughter, Jeanette Saskowski, Marta A. Crispens, Howard W. Jones III, Samuel James, Oluwafunmilayo B. Adebayo, Sarah A. Fletcher, Andrew J. Wilson, Annie Y. Liu, Joseph Roland, James C. Slaughter, Jeanette Saskowski, Marta A. Crispens, Howard W. Jones III, Samuel James, Oluwafumilayo A. Adebayo, Sarah A. Fletcher, and Andrew J. Wilson

Précis: There remains great interest in determining general strategies to overcome resistance to platinum compounds that are used very widely to treat cancer, including ovarian cancer.
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**Prevention and Epidemiology**

- Genetic Ablation of the Fatty Acid-Binding Protein FABP5 Suppresses HER2-Induced Mammary Tumorigenesis
- PanIN-Specific Regulation of Wnt Signaling by HIF2α during Early Pancreatic Tumorigenesis
- Enhanced Radiation Sensitivity in HPV-Positive Head and Neck Cancer
- Pathway-Based Serum microRNA Profiling and Survival in Patients with Advanced Stage Non–Small Cell Lung Cancer
- A 20-Year Prospective Study of Plasma Prolactin as a Risk Marker of Breast Cancer Development

**Therapeutics, Targets, and Chemical Biology**

- Novel Recombinant Human B7-H4 Antibodies Overcome Tumoral Immune Escape to Potentiate T-Cell Antitumor Responses
- Transcription Poisoning by Topoisomerase I Is Controlled by Gene Length, Splice Sites, and miR-142-3p
- C-RAF Mutations Confer Resistance to RAF Inhibitors
- Pivotal Role of the Lipid Raft SK3–Orail Complex in Human Cancer Cell Migration and Bone Metastases
- Docetaxel Conjugate Nanoparticles That Target α-Smooth Muscle Actin–Expressing Stromal Cells Suppress Breast Cancer Metastasis
Aptamer Identification of Brain Tumor-Initiating Cells
Youngmi Kim, Quilian Wu, Petra Hamerlik, Masahiro Hitomi, Andrew E. Sloan, Gene H. Barnett, Robert J. Weil, Patrick Leahy, Anita B. Hjelmeland, and Jeremy N. Rich

Precis: This work illustrates a general method to prospectively isolate tumor-initiating cells, the imaging and targeting of which may be important for improving therapeutic outcomes in individual patients.

Loss of p120-Catenin Induces Metastatic Progression of Breast Cancer by Inducing Anoikis Resistance and Augmenting Growth Factor Receptor Signaling

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.

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: 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.
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.