Highlights from Recent Cancer Literature

From Integrative Genomics to Therapeutic Targets
Rachael Natrajan and Paul Wilkerson

HER2 and Breast Cancer Stem Cells: More than Meets the Eye
Hasan Korkaya and Max S. Wicha

APOBEC3 Cytidine Deaminases in Double-Strand DNA Break Repair and Cancer Promotion
Roni Nowarski and Moshe Kotler

Immune Infiltrates Are Prognostic Factors in Localized Gastrointestinal Stromal Tumors

Kinetic Modeling-Based Detection of Genetic Signatures That Provide Chemoresistance via the E2F1-p73/DNp73-miR-205 Network
Julio Vera, Ulf Schmitz, Xin Lai, David Engelmann, Faiz M. Khan, Olaf Wolkenhauer, and Brigitte M. Putzer

Mathematical Modeling of Tumor Cell Proliferation Kinetics and Label Retention in a Mouse Model of Lung Cancer
Yanyan Zheng, Helen Moore, Alexandra Piryatinska, Trinidad Solis, and E. Alejandro Sweet-Cordero

Booster Vaccinations against Cancer Are Critical in Prophylactic but Detrimental in Therapeutic Settings
Alessia Ricupito, Matteo Grioni, Arianna Calcinotto, Rodrigo Hess Michelini, Renato Longhi, Anna Mondino, and Matteo Bellone

MICROENVIRONMENT AND IMMUNOLOGY

BoostervaccinationsagainstCancer
AreCriticalinProphylacticbutDetrimentalinTherapeuticSettings
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Prices: This study challenges the notion that repeatedly boosting tumor-bearing subjects with a vaccine can sustain protective, long-lasting antitumor immunity, instead showing that certain prime-boost strategies actually drive T-cell exhaustion rather than expansion and memory.
A Novel Model for Evaluating Therapies Targeting Human Tumor Vasculature and Human Cancer Stem–like Cells
Daniela Burgos-Ojeda, Karen McLean, Shoumei Bai, Heather Pulaski, Yusong Gong, Ines Silva, Karl Skorecki, Maty Tzukerman, and Ronald J. Buckanovich

Precis: There remains a great need for preclinical models that can more accurately predict clinical responses to novel experimental therapeutic agents in development.

Enhanced Effector Responses in Activated CD8+ T Cells Deficient in Diacylglycerol Kinases

Precis: Targeting of diacylglycerol kinases offers a general approach to enhance the function of chimeric antigen receptor T cells (CART cells), a promising new strategy for cancer immunotherapy.

SOCS3 Transactivation by PPARγ Prevents IL-17–Driven Cancer Growth
Hélène Berger, Frédérique Végran, Madjid Chikh, Federica Gilarde, Sylvain Ladoire, Hélène Bugaut, Grégoire Magnot, Fanny Chalmin, Mélanie Bruchard, Valentin Derangère, Angélique Chefriaux, Cédric Rébé, Bernhard Ryffel, Caroline Pot, Aziz Ilichami, Béatrice Desvergne, François Ghiringhelli, and Lionel Apetoh

Precis: This study reveals new mechanistic insights into how inflammation supports cancer, and how blocking certain inflammatory pathways can restrict cancer.

Dual Blockade of PD-1 and CTLA-4 Combined with Tumor Vaccine Effectively Restores T-Cell Rejection
Jaikumar Duraiswamy, Karen M. Kaluza, Gordon J. Freeman, and George Coukos

Precis: Combined checkpoint blockade is synergistic and strongly augments the efficacy of vaccination to restore T-cell exhaustion and promote tumor rejection.

BMP-6 in Renal Cell Carcinoma Promotes Tumor Proliferation through IL-10–Dependent M2 Polarization of Tumor-Associated Macrophages
Jae-Ho Lee, Geum Taek Lee, Seung Hyo Woo, Yun-Sok Ha, Seok Joo Kwon, Wun-Jae Kim, and Isaac Yi Kim

Precis: Elevated IL-10 levels have been broadly associated with tumor tolerance and immune escape, but the basis for IL-10 upregulation and its critical cellular targets in tumors have not been fully clear.

YAP/TEAD–Mediated Transcription Controls Cellular Senescence
Qi Xie, Jing Chen, Han Feng, Shengyi Peng, Ursula Adams, Yujie Bai, Li Huang, Ji Li, Junjian Huang, Songshu Meng, and Zengqiang Yuan

Precis: These findings offer general significance in cancers in which cellular senescence acts as a tumor suppressor, with implications for novel therapeutic approaches to stanch tumor growth.

ATF3 Suppresses Metastasis of Bladder Cancer by Regulating Gelsolin-Mediated Remodeling of the Actin Cytoskeleton
Xiangliang Yuan, Liang Yu, Junhua Li, Guohua Xie, Tingting Rong, Liang Zhang, Jianhua Chen, Qiaoqiong Meng, Aaron T. Irving, Die Wang, Elisabeth D. Williams, Jun-Ping Liu, Anthony J. Sadler, Bryan R.G. Williams, Lixong Shen, and Dakang Xu

Precis: Mechanistic findings identify a transcription factor that suppresses metastasis of bladder cancer cells, suggesting new markers and strategies to define and address aggressive bladder tumors.

Nkx2-8 Downregulation Promotes Angiogenesis and Activates NF-κB in Esophageal Cancer
Chuyong Lin, Libing Song, Hui Gong, Aibin Liu, Xi Lin, Juebing Wu, Mengfeng Li, and Jun Li

Precis: These findings define a new tumor suppressor in esophageal cancer, the downregulation of which contributes to NF-κB activation and tumor angiogenesis.

Targeting ROR1 Inhibits Epithelial–Mesenchymal Transition and Metastasis
Bing Cui, Suping Zhang, Liguang Chen, Jianqiang Yu, George F. Widhopf II, Jessie-F. Fecteau, Laura Z. Rassenti, and Thomas J. Kipps

Precis: As a pivotal step in what converts curable benign tumors to untreatable malignant cancers, the cellular process of EMT and the key factors regulating it remain an important focus of attention in identifying cancer-specific therapies.
**TUMOR AND STEM CELL BIOLOGY**

**Inhibition of c-Met Reduces Lymphatic Metastasis in RIP-Tag2 Transgenic Mice**
Barbara Sennino, Toshina Ishiguro-Oonuma, Brian J. Schriver, James G. Christensen, and Donald M. McDonald

**Precis:** VEGF inhibition increases expression of c-Met, which can promote lymph node metastases, with consequences for understanding how resistance arises to antiangiogenic therapies.

**Antioxidant Enzymes Mediate Survival of Breast Cancer Cells Deprived of Extracellular Matrix**

**Precis:** This study offers evidence that blocking antioxidant enzymes may help kill cancer cells that are poised to metastasize, a finding that is counterintuitive in light of a large body of literature encouraging antioxidant treatments to prevent cancer.

**MTA1 Promotes STAT3 Transcription and Pulmonary Metastasis in Breast Cancer**

**Precis:** Endogenous levels of a prometastatic transcriptional coregulator are sufficient to support its function in metastasis, whether or not it is overexpressed in cancer.
DDB2 Suppresses Epithelial-to-Mesenchymal Transition in Colon Cancer
Nilotpal Roy, Prashant V. Bommi, Uppoor G. Bhat, Shaumick Bhattacharjee, Indira Elangovan, Jing Li, Krushna C. Patra, Dragana Kopanja, Adam Blunier, Richard Benya, Srilata Bagchi, and Pradip Raychaudhuri

Precis: A nucleotide excision repair protein is found to function as an inhibitor of EMT, a phenotypic change in transformed epithelial cells that facilitates invasion and metastasis, suggesting a direct link between these processes during tumorigenesis.

GDNF–RET Signaling in ER-Positive Breast Cancers Is a Key Determinant of Response and Resistance to Aromatase Inhibitors
Andrea Morandi, Lesley-Ann Martin, Qiong Gao, Sunil Pancholi, Alan Mackay, David Robertson, Marketa Zvelebil, Mitch Dowsett, Ivan Plaza-Menacho, and Clare M. Isacke

Precis: This study addresses the clinical challenge of therapeutic resistance in oncology, in this case by defining an important tractable pathway of resistance to aromatase inhibitors used to fight ER-positive breast cancer.

Sox2 Requirement in Sonic Hedgehog-Associated Medulloblastoma
Julia Ahlfeld, Rebecca Favaro, Pierfrancesco Pagella, Hans A. Kretzschmar, Silvia Nicolis, and Ulrich Schuller

Precis: This study links a core pathogenic driver of an aggressive pediatric tumor to a central regulator of cancer stem-like function, with potential therapeutic implications.