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4270  Cancer Affects microRNA Expression, Release, and Function in Cardiac and Skeletal Muscle
Daohong Chen, Chirayu P. Goswami, Riesa M. Burnett, Manjushree Anjanappa, Poornima Bhat-Nakshatri, William Müller, and Harikrishna Nakshatri

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**Précis:** This study offers evidence that a circulating microRNA could serve as a surrogate of the effects of cancer on microRNA expression in distant organs.
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4282  **Germline Mutations in BAP1 Impair Its Function in DNA Double-Strand Break Repair**  
Ismail Hassan Ismail, Riley Davidson, Jean-Philippe Gagné, Zhi Zhong Xu, Guy G. Poirier, and Michael J. Hendzel  

**Précis:** This study provides a missing link in the DNA damage response and provides a mechanistic explanation for how BAP1 functions as a tumor suppressor gene.

4295  **PME-1 Modulates Protein Phosphatase 2A Activity to Promote the Malignant Phenotype of Endometrial Cancer Cells**  
Ewa Wandzioch, Michelle Pusey, Amy Werda, Sophie Bail, Aishwarya Bhaskar, Mariya Nestor, Jing-Jing Yang, and Lyndi M. Rice  

**Précis:** These findings identify a methyltransferase for the protein phosphatase PP2A as a modifier of cancer development and a theranostic target in endometrial tumors.

4306  **AR-Regulated TWEAK-FN14 Pathway Promotes Prostate Cancer Bone Metastasis**  
Juanjuan Yin, Yen-Nien Liu, Heather Tillman, Ben Barrett, Stephen Hewitt, Kris Yaya, Lei Fang, Ross Lake, Eva Corey, Colm Morrissey, Robert Vessella, and Kathleen L. Rice  

**Précis:** These findings identify a TNF receptor family member as a candidate therapeutic agent and imaging target in castrate-resistant prostate cancer.

4318  **B-cell Expansion and Lymphomagenesis Induced by Chronic CD40 Signaling Is Strictly Dependent on CD19**  
Caroline Hojer, Samantha Frankenberger, Lothar J. Strobl, Samantha Feicht, Kristina Djermanovic, Franziska Jagdhuber, Cornelia Homig-Holzel, Uta Ferch, Jürgen Ruland, Klaus Rajewsky, and Ursula Zimber-Strobl  

**Précis:** CD19 acts as a coreceptor not only for the B-cell receptor but also for CD40, mediating critical survival and proliferation signals in B-cell tumors.

4329  **IL4 Receptor ILR4α Regulates Metastatic Colonization by Mammary Tumors through Multiple Signaling Pathways**  
Katherine T. Venmar, Kathy J. Carter, Daniel G. Hwang, E. Ashley Dozier, and Barbara Fingleton  

**Précis:** Although the IL4 receptor is usually associated with immune cells, it has a significant role in controlling the metastatic capabilities of breast tumor cells, with immediate implications for targeting this receptor as a strategy to treat advanced breast cancer.

4341  **miR-21 Induces Myofibroblast Differentiation and Promotes the Malignant Progression of Breast Phyllodes Tumors**  
Chang Gong, Yan Nie, Shaohua Qu, Jian-You Liao, Xiuying Cui, Herui Yao, Yunjie Zeng, Fengxi Su, Erwei Song, and Qiang Liu  

**Précis:** The perspective afforded by this study confirms the suspicion that prospects for effective immunotherapy are far more likely to emerge from targeting multiple tumor antigens than single tumor antigens.

4353  **Snail Recruits Ring1B to Mediate Transcriptional Repression and Cell Migration in Pancreatic Cancer Cells**  
Jiangzhi Chen, Hong Xu, Xiqun Zou, Jiamin Wang, Yi Zhu, Hao Chen, Baiyong Shen, Xixing Deng, Aiwu Zhou, Y. Eugene Chin, Frank J. Rauscher, III, Chenghong Peng, and Zhaojuan Hou  

**Précis:** This study unravels an epigenetic mechanism underlying transcriptional repression by a core regulator of EMT in pancreatic cancer, suggesting new candidate theranostic targets in this disease.

4364  **AEG-1 Regulates Retinoid X Receptor and Inhibits Retinoid Signaling**  

**Précis:** This article presents evidence of a functional biomarker in cancer cell responses to retinoic acids used for therapy, with implications for screening procedures before these agents are prescribed for patients.

4378  **In Vivo Regulation of Human Glutathione Transferase GSTP by Chemopreventive Agents**  
Colin J. Henderson, Aileen W. McLaren, and C. Roland Wolf  

**Précis:** These findings suggest how dietary components modulate an enzyme that is critical for determining cancer susceptibility and the outcome of chemotherapy treatments.
Germline Mutation of Bap1 Accelerates Development of Asbestos-Induced Malignant Mesothelioma

Jinfei Xu, Yuwaraj Kadariya, Mitchell Cheung, Jianming Pei, Jacqueline Talarchek, Eleonora Sementino, Yinfei Tan, Craig W. Menges, Kathy Q. Cai, Samuel Litvin, Hongzhuang Peng, Jayashree Karar, Frank J. Rauscher, and Joseph R. Testa

Précis: Unbiased genetic findings demonstrate that BAP1 mutation carriers are predisposed to asbestos-induced mesothelioma, a hazard of certain domiciles and workplaces, where asbestos exposure would greatly synergize with inherited mutations of BAP1 in elevating risk.

Increased Dietary Vitamin D Suppresses MAPK Signaling, Colitis, and Colon Cancer

Stacey Meeker, Audrey Seamons, Jisun Paik, Piper M. Treuting, Thea Brabb, William M. Grady, and Lillian Maggio-Price

Précis: In a mouse model of colitis and colon cancer, increasing dietary vitamin D prevented inflammatory responses involved in early stages of carcinogenesis, with potential clinical implications for chemoprevention by vitamin D.

Inhibition of miR17 and miR20a by Oridonin Triggers Apoptosis and Reverses Chemoresistance by Derepressing BM-S

Hengyou Weng, Huilin Huang, Bowen Dong, Panpan Zhao, Hui Zhou, and Lianghu Qu

Précis: These results suggest the combined use of chemotherapy drugs with a natural microRNA-targeting agent to reverse cancer chemoresistance.

ASC-J9 Suppresses Renal Cell Carcinoma Progression by Targeting an Androgen Receptor–Dependent HIF2α/VEGF Signaling Pathway

Dalin He, Lei Li, Guodong Zhu, Liang Liang, Zhenfeng Guan, Luke Chang, Yuan Chen, Shuyuan Yeh, and Chawnshang Chang

Précis: These findings may explain why men have a higher incidence of kidney cancer than women, by revealing contributions of the androgen receptor that offers a new candidate target in this disease.

Afatinib Enhances the Efficacy of Conventional Chemotherapeutic Agents by Eradicating Cancer Stem–like Cells

Xiao-kun Wang, Jie-hua He, Jing-hong Xu, Sheng Ye, Fang Wang, Hui Zhang, Zhen-cong Huang, Kenneth Kin Wah To, and Li-wu Fu

Précis: These findings suggest use of an approved tyrosine kinase inhibitor to improve the efficacy of conventional chemotherapeutic drugs by improving eradication of cancer stem-like cells, with immediate clinical implications.

Increased Dietary Vitamin D Suppresses MAPK Signaling, Colitis, and Colon Cancer

Stacey Meeker, Audrey Seamons, Jisun Paik, Piper M. Treuting, Thea Brabb, William M. Grady, and Lillian Maggio-Price

Précis: In a mouse model of colitis and colon cancer, increasing dietary vitamin D prevented inflammatory responses involved in early stages of carcinogenesis, with potential clinical implications for chemoprevention by vitamin D.

NSAID Use Reduces Breast Cancer Recurrence in Overweight and Obese Women: Role of Prostaglandin–Aromatase Interactions


Précis: This study deepens the potential connections between obesity-associated inflammation and breast cancer, with implications for a straightforward treatment and prevention strategy in estrogen-positive cancers, which are the most common clinically.

Selective and Potent Akt Inhibition Triggers Anti-Myeloma Activities and Enhances Fatal Endoplasmic Reticulum Stress Induced by Proteasome Inhibition

Naoya Mimura, Teru Hideshima, Toshiyasu Shimomura, Riko Suzuki, Hiroto Ohguchi, Ola Rizq, Shohei Kikuchi, Yasuhiro Yoshida, Francesca Cottini, Jana Jakubikova, Diana Cirstea, Guilu Gorgun, Jiro Minami, Yu-Tzu Tai, Paul G. Richardson, Tenuhiro Usui, Atsushi Iwama, and Kenneth C. Anderson

Précis: These results offer a preclinical proof of concept for the use of a novel Akt inhibitor in treating multiple myeloma, alone or in combination with proteasome inhibitors that are currently approved for this use.
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<td>Eph tyrosine kinases controlling cell attraction and repulsion forces involved in migration have been challenging to position for therapeutic invention, but this article suggests an approach to effectively target EphA3 in solid tumors as a novel type of generalized therapy for malignant tumors.</td>
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<td>Yulei Zhao, Prem Khanal, Paul Savage, Yi-Min She, Terry D. Cyr, and Xiaolong Yang</td>
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<td>Overexpression of an enzyme that degrades cell surface heparan sulfate is associated with malignant progression, but this study shows that it is also important at early stages of tumor development, reinforcing its candidacy as a therapeutic target.</td>
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ABOUT THE COVER

Expression of the multidrug resistance protein ABCG2 confers chemoresistance to CSC where it serves as a potential biomarker and therapeutic target. Afatinib, a small molecule inhibitor of the tyrosine kinases EGFR, HER2, and HER4, can enhance the antitumor effect of the DNA damaging drug topotecan in vitro and in vivo. Immunofluorescence microscopic analysis showed that afatinib significantly decreased the cell surface expression of ABCG2 in a concentration-dependent manner. For details, see article by X.-K. Wang and colleagues on page 4431.

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