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**MOLECULAR AND CELLULAR PATHOBIOLOGY**

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*These findings define a new tumor suppressor in esophageal cancer, the downregulation of which contributes to NF-κB activation and tumor angiogenesis.*
**DOG1 Regulates Growth and IGFBP5 in Gastrointestinal Stromal Tumors**

Susanne Simon, Florian Grabellus, Loretta Ferrera, Luis Galetta, Benjamin Schwindenhammer, Thomas Mühlendberg, Georg Taeger, Grant Eilers, Juergen Treckmann, Frank Breitenbuecher, Martin Schuler, Takahiro Taguchi, Jonathan A. Fletcher, and Sebastian Bauer

**Précis:** These findings reveal a novel oncogenic mechanism in GIST that highlights the importance of the tumor microenvironment as a therapeutic target in this disease.

---

**Pak1 Kinase Links ErbB2 to β-Catenin in Transformation of Breast Epithelial Cells**

Luis E. Arias-Romero, Olga Villamar-Cruz, Min Huang, Klaus P. Hoeflich, and Jonathan Chernoff

**Précis:** Important mechanistic insights suggest new therapeutic strategies to treat breast cancers that involve HER2 overexpression.

---

**ATR Inhibition Broadly Sensitizes Ovarian Cancer Cells to Chemotherapy Independent of BRCA Status**

Catherine J. Huntoon, Karen S. Flatten, Andrea E. Wahner Hendrickson, Amelia M. Huerbs, Shari L. Sutor, Scott H. Kaufmann, and Larry M. Karnitz

**Précis:** Findings that directly affect clinical treatment of BRCA1/2-deficient cancer cells are provided in this study, which addresses long-standing questions of how to leverage these conditions to improve effective therapeutic targeting.

---

**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

**Précis:** 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**


**Précis:** 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.

---

**FGFR1 Is Essential for Prostate Cancer Progression and Metastasis**

Feng Yang, Yongyou Zhang, Steven J. Ressler, Michael M. Ittmann, Gustavo E. Ayala, Truong D. Dang, Fen Wang, and David R. Rowley

**Précis:** Fibroblast growth factor signaling in prostate cancer is emerging as an important area of therapeutic potential, as shown in this study of FGFR1, which suggests a rationale to attack metastatic tumors.

---

**Androgen Receptor-Independent Function of FoxA1 in Prostate Cancer Metastasis**

Hong-Jian Jin, Jonathan C. Zhao, Irene Ogden, Raymond C. Bergan, and Jindan Yu

**Précis:** This study may explain why recurrent FoxA1 mutations that have been found to occur in prostate cancer contribute to malignant progression in this disease.

---

**NF-κB Regulates Radioresistance Mediated By β1 Integrin in Three-Dimensional Culture of Breast Cancer Cells**

Kazi Mokim Ahmed, Hui Zhang, and Catherine C. Park

**Précis:** The results of this study suggest a novel approach to radiosensitize malignant breast cancers by targeting a forward feedback cell adhesion pathway.

---

**ING5 Is a Tip60 Cofactor That Acetylates p53 in Response to DNA Damage**

Nansong Liu, Jiadong Wang, and Catherine C. Park

**Précis:** This study illuminates one of the mechanisms through which cells determine whether to undergo cell-cycle arrest or apoptosis after p53 activation.

---

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


**Précis:** 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

Précis: 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

Précis: 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 Schüller

Précis: 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.

ABOUT THE COVER
Inhibition of VEGF signaling reduces angiogenesis and slows tumor growth, but can also promote lymph node metastasis in some preclinical models. Studies of RIP-Tag2 transgenic mice revealed that inhibition of VEGF signaling by a function blocking anti-VEGF antibody or the receptor tyrosine kinase inhibitor sunitinib increased the number of intratumoral lymphatics, the proportion of lymphatics with tumor cells inside, and the incidence of lymph node metastasis. After the treatment, c-Met was upregulated in lymphatics in and around the tumors. Importantly, inhibition of c-Met by PF-04217903 administered with the angiogenesis inhibitor significantly reduced the abundance of intratumoral lymphatics, tumor cells inside lymphatics, and lymph node metastases. For details, see article by Sennino and colleagues on page 3692.