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557 Telomerase Suppresses Formation of ALT-Associated Single-Stranded Telomeric C-Circles
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CELL DEATH AND SURVIVAL

568 PPP2R2C Loss Promotes Castration-Resistance and Is Associated with Increased Prostate Cancer-Specific Mortality

CHROMATIN, GENE, AND RNA REGULATION

593 mda-7/IL-24 Expression Inhibits Breast Cancer through Upregulation of Growth Arrest-Specific Gene 3 (gas3) and Disruption of β1 Integrin Function
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616 RAS/MEK-Independent Gene Expression Reveals BMP2-Related Malignant Phenotypes in the Nf1-Deficient MPNST
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628 CDCP1 Regulates the Function of MT1-MMP and Invadopodia-Mediated Invasion of Cancer Cells
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638 Human Lung Epithelial Cells Progressed to Malignancy through Specific Oncogenic Manipulations

SIGNAL TRANSDUCTION

651 The Tyrosine Phosphatase SHP2 Regulates Focal Adhesion Kinase to Promote EGF-Induced Lamellipodia Persistence and Cell Migration
Zachary R. Hartman, Michael D. Schaller, and Yehenew M. Agazie
ABOUT THE COVER

Nonmalignant immortalized human bronchial epithelial cells (HBECs, containing hTERT and CDK4 providing a bypass of p16 – two common oncogenic changes found in lung cancer) can be progressed to fully malignant cells capable of in vivo tumor formation following the introduction of defined oncogenic alterations (such as high levels of oncogenic KRAS, p53 knockdown, with or without exogenous c-myc expression) mimicking genetic alterations commonly found in non-small cell lung cancer. Recent genomic data shows large number of sequence altering mutations in human lung cancers requiring sorting out of "passenger" and "driver" oncogenic changes. The HBEC preclinical in vitro model provides a way to test these candidates and identify the minimal, most crucial set of genetic alterations required for full malignant transformation of a bronchial epithelial cell. NOD/SCID xenograft tumors of cells with similar oncogenic changes amazingly led to multiple different lung cancer histologies (adenocarcinoma, squamous carcinoma, adeno-squamous and large cell carcinoma) indicating that factors other than oncogenic changes dictate histology. Shown here is one of the HBEC-p53,KRAS tumors that differentiated into typical lung adenocarcinoma as demonstrated by Alcian-Blue Periodic Acid Schiff (PAS) stain where mucins are stained with Alcian blue (original magnification at 10X). For examples of the other histologies and details, see article by Sato, Larsen, and colleagues on page 638.