Molecular Cancer Research Highlights

June 2010 • Volume 8 • Number 6

Selected Articles from This Issue

USP26 is a Regulator of Androgen Receptor Signaling

Dirac and Bernards Page 844

Ubiquitination significantly contributes to regulation of many cellular signaling pathways. Dirac and Bernards used a siRNA-mediated genetic screening approach to identify novel deubiquitinating enzymes in the androgen receptor (AR) signaling pathway, which is implicated in prostate cancer development. They found that USP26 uses several of its nuclear receptor interaction motifs to bind the AR. USP26 regulates AR activity by counteracting hormone-induced ubiquitination of AR. Dirac and Bernards propose that USP26 is part of multi-component AR transcriptional complexes controlling AR target gene activation and speculate that altered USP26 expression levels may contribute to aberrant AR signaling and thus prostate cancer development.

Sprouty-4 Inhibits Transformed Cell Growth in NSCLC

Tennis *et al.* Page 833

The receptor tyrosine kinase inhibitor Sprouty-4 has previously been shown to antagonize growth factor signaling and is involved in lung development. Tennis and colleagues report that Sprouty-4 is lost in non–small cell lung cancer cell lines, suggesting that it can act as a tumor suppressor. This article shows that Sprouty-4 inhibits cell growth, migration, invasion, and EMT. Tennis and coworkers also describe regulation of Sprouty-4 by Wnt7A/Fzd9 signaling through PPARγ. A new role for Sprouty-4 is indicated by these data and presents a possible therapeutic target for non–small cell lung cancer.

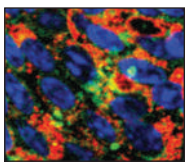
PCAF and Cisplatin Resistance

Hirano *et al* Page 864

Drug and apoptosis resistance are two sides of the same coin. Cisplatin resistance is influenced by several factors that affect drug accumulation, levels of cellular thiols, and DNA repair activity. The role of histone acetyltransferase (HAT) gene expressions in the development of drug resistance has not been extensively studied. It has been previously shown that HAT genes such as *CLOCK* and *TIP60* involve cisplatin resistance through glutathione biosynthesis and DNA repair. Hirano et al reported that another HAT gene, *PCAF,* is overexpressed in cisplatin-resistant cells and endowed an antiapoptotic phenotype through enhanced E2F1 expression.

Phospho-K8 in Mammary Cells and Tumors

Kongara *et al.* Page 873



The essential autophagy regulator beclin 1 is monoallelically deleted in many breast tumors and beclin $1^{+/-}$ mice exhibit mammary hyperplasias. To explore the role of autophagy in mammary gland biology and breast cancer, Kongara et al. examined how autophagy-competent and -defective mammary epithelial cells respond to metabolic stress and found that autophagy defects are associated with elevated endoplasmic reticulum and oxidative stress, and abnormal keratin accumulation. Similar findings were observed in autophagy-defective mammary glands, in allograft mammary tumors, and in human breast tumors. Furthermore, phospho(Ser73)-K8 was identified as a potential marker for autophagy functional status in breast cancer.

Molecular Cancer Research

Highlights of This Issue

Mol Cancer Res 2010;8:807.