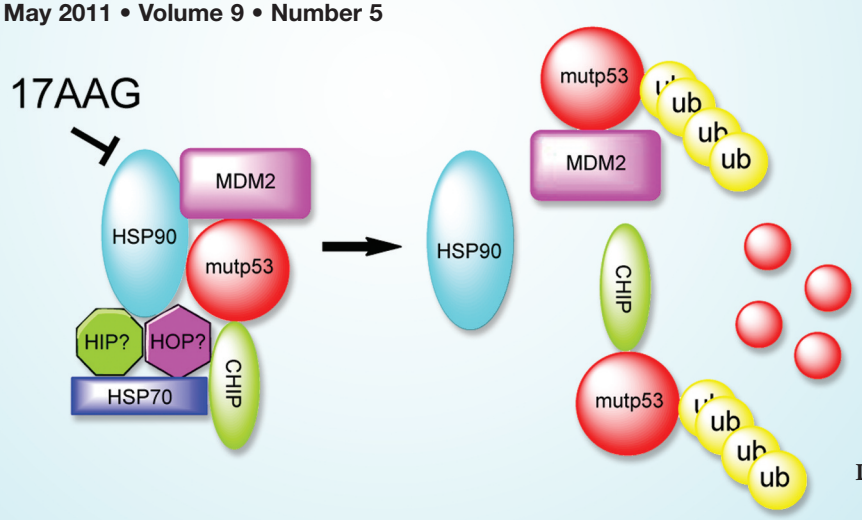
Molecular Cancer Research **Highlights**

May 2011 • Volume 9 • Number 5

Selected Articles from This Issue



HSP90-Mediated MDM2 and CHIP Inactivation Causes Mutant p53 Stabilization in Cancer

Li *et al.* Page 577

The tight control of wild-type p53 by MDM2 in normal cells is permanently lost in tumors with mutant p53 that exhibit dramatic constitutive hyperstabilization, critical for mutp53's oncogenic gain-of–function. Li and coworkers show that mutp53 stabilization is caused by stable complexes with the HSP90 chaperone machinery that inhibits the MDM2 and CHIP E3 ligase activity. Interference with HSP90 destroys the complex, liberates mutp53 and reactivates MDM2 and CHIP to robustly degrade mutp53. HSP90 interference with 17AAG also induces stronger cell death in mutp53 than in wtp53 cancer cells. This suggests that pharmacologic suppression of mutp53 levels in established cancers might achieve clinically significant effects.

Fibulin-5 in Metastases

Møller *et al.* Page 553

Tumor-associated fibroblasts constitute an important part of the tumor stroma. It has been shown that they are essential in stimulation of the metastatic spread of tumor cells from the primary site. Here we show that fibroblasts are also instrumental in stimulating metastasis formation during organ colonization. Gene expression profiling of fibroblasts identified genes whose expression is modulated by factors derived from tumor cells. One of them encodes for the matricellular protein Fibulin-5, which inhibits metastatic organ colonization by regulating the ability of fibroblasts to invade the extracellular matrix, hence generating a favorable microenvironment for metastasis development.

Surface Proteome Signature Predicts Tumor Drug Resistance

Cain *et al.* Page 637

The lack of biomarkers that specify cancers with different cellular properties is a critical unmet need in cancer diagnosis. Cain and colleagues report surface proteome signature (SPS) technology. SPS uses a phage display library directed to the surface of HT-1080 fibrosarcoma cells for a differential immunocytochemistry screen to detect differences between closely related cancer cell lines. SPS identified CD44, the hyaluronan receptor, as a biomarker differentially expressed between two cell lines thought to differ in drug resistance due solely to the expression of the drug efflux pump, P-Glycoprotein. Additionally, they showed that CD44 increases drug resistance independent of P-Glycoprotein.

CARM1 and β-Catenin in Aberrant Growth of Colon Cancer Cells

Ou *et al.* Page 660

Aberrant activation of Wnt/β-catenin signaling promotes oncogenesis by increasing expression of oncogenes and is, therefore, critical for the etiology of colorectal cancer. Occupancy of β-catenin at promoters of Wnt target genes drives transcription, but the mechanism of β-catenin action remains poorly understood. Here, Ou and coworkers show that the arginine methyltransferase and transcriptional coactivator CARM1 is recruited by β-catenin to Wnt target genes as an important positive modulator of Wnt/β-catenin transcription and neoplastic transformation. Abnormal expression of CARM1 was previously linked to human colorectal cancers. Thus, CARM1 is a potential new target for treatment of colorectal cancers involving aberrantly activated Wnt/β-catenin signaling.

Molecular Cancer Research

Highlights of This Issue

Mol Cancer Res 2011;9:529.