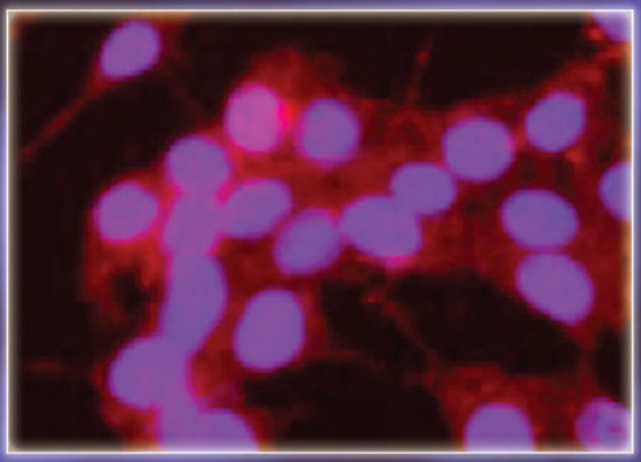
Molecular Cancer Research **Highlights**

October 2010 • Volume 8 • Number 10 Selected Articles from This Issue

Hsp27 Drives p21 in DNA-Damaged Cancer Cell and Decides Its Fate

Kanagasabai *et al.* _____Page 1399

Survival or death of cancer cells after inducing DNA damage has always been a challenge to predict because what decides the survival or death of DNA-damaged cell is not completely understood. Kanagasabai and coworkers have found a new mechanism by which a small heat shock protein, Hsp27, can modulate the dynamics of p21 translocation from cytoplasm to nucleus, leaving the DNA-damaged cell either to survive or die. This novel finding may provide new insights in understanding how cancer cells survive after drug treatment.



EphB4/EphrinB2 Interactions during Metastatic Dissemination

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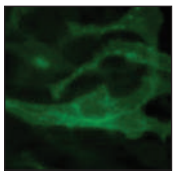
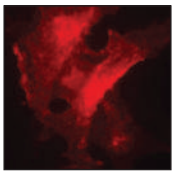


It has been more than 100 years since Stephen Paget established the 'seed and soil' theory of tumor spread and metastasis, yet, the molecular mechanisms underlying site-specific metastasis are still poorly understood. Héroult and colleagues have taken the multistep metastatic cascade apart in single steps to focus specifically on the mechanisms of systemic spread of tumor cells and homing to organ-specific molecular determinants of vascular endothelial cells. Using sensitive luciferase-based cell tracing techniques, the study showed that tumor cell–expressed EphB4 is, in a forward signaling–dependent manner, capable of mediating the site-specific metastatic dissemination to ephrinB2-positive vascular beds.

Roles of Rac1 and Arf6 in Ras-Induced Cell Death

Bhanot *et al.* _____Page 1358

Methuosis is an unconventional form of cell death characterized by extreme cytoplasmic vacuolization. It can be induced in glioblastoma and other cancer cells by expression of the active form of H-Ras. Bhanot and coworkers show that this novel effect of Ras entails simultaneous activation of Rac1 and inactivation of Arf6, two GTPases that function in endosomal trafficking. Reduced Arf6 activity appears to be mediated through an interaction between Rac1 and the Arf GTPase-activating protein, GIT1. Further clarification of the signals that drive methuosis may prove useful for devising new approaches to kill cancer cells that are refractory to apoptosis.



ErbB4 Interactions with Kap1

Gilmore-Hebert *et al.* _____Page 1388

EGFR, ErbB2, and ErbB3 are cancer drivers and therapeutic targets, however, ErbB4 has both negative and positive roles in cancer. This may be explained by diverse biological activities of ErbB4 spliced isoforms. Some isoforms are cleaved to release an active intracellular domain that homes to the nucleus. Gilmore-Hebert and colleagues identified proteins associated with nuclear ErbB4 including Kap1, a corepressor of transcription and coregulator, with MDM2, of p53. Kap1 reduces ERBB4 transcription and modulates the expression of genes that are regulated by ErbB4. Upregulation of ErbB4 and suppression of MDM2 enhance and accelerate the accumulation of p21CIP1 in response to DNA damage. Overall, these findings further substantiate the role of ErbB4 in conjoint regulation of growth factor signaling and DNA damage responses and add to the growing number of links between canonical growth regulatory pathways and DNA damage response systems.

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Mol Cancer Res 2010;8:1295.