FEATURES

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Molecular Chaperones in Breast Cancer

1096

Stuart K. Calderwood and Jianlin Gong

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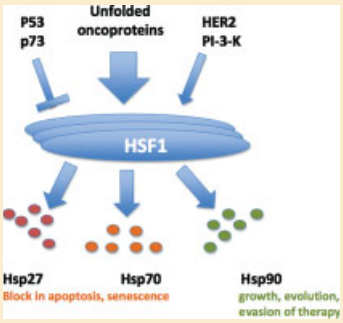

The evolution of mammary carcinoma is fueled by alterations in the tumor proteome, including elevated expression of mutant oncoproteins, the molecular mediators of cancer. Such a radical transformation in the protein landscape requires the increased expression of molecular chaperones in tumors. Molecular chaperones can interact with proteins with unstable structure or reduced solubility and deter their breakdown through the proteosome. Mammary cancer cells become progressively dependent on molecular chaperones such as heat shock proteins (HSP) 27, 70 and 90 to stabilize the malignant proteome, protect the structures of oncogenes and maintain tumor progression. These effects, in turn, require the upregulation of HSP transcription in mammary cancer cells by activation of heat shock factor 1(HSF1), the major regulator of HSP expression. The dependency of breast cancer cells on HSF1 and the HSPs therefore indicates the continuing development of novel agents to target these molecules, destabilize the malignant proteome and inhibit the growth and viability of mammary cancer cells.

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miRNA Regulates Mitochondrial Function

1104

Peifeng Li, Jianqing Jiao, Guifeng Gao, and Bellur S. Prabhakar

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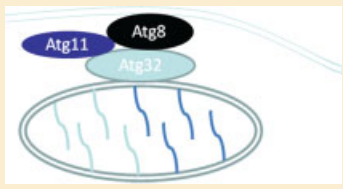

Mitochondria play an important role in controlling the cellular physiology, and mitochondrial dysfunction can cause pathology. microRNAs (miRNAs) are a class of small noncoding RNAs about 22 nucleotides long, and they can bind to the 3′-untranslated region (3′-UTR) of mRNAs, thereby inhibiting mRNA translation or promoting mRNA degradation. In this review Li *et al.* summarize the role of miRNAs in regulating mitochondrial activity. A fundamental function of mitochondria is to produce ATP through oxidative phosphorylation. Interestingly, miRNAs can affect mitochondrial metabolism including the process of ATP generation. miRNAs play a critical role in regulating mitochondria-mediated apoptosis through the regulation of proteins that are involved in the process. Mitochondria constantly undergo biogenesis, fusion and fission, and they form dynamic networks that are necessary for the maintenance of organelle fidelity. These processes are also regulated by miRNAs. Autophagy is a process of catabolism of cellular components and is necessary for the maintenance of cell homeostasis; selective degradation of mitochondria by this process is termed mitophagy. Recent studies have begun to explore the role of miRNA in mitophagy. This review by Li *et al.* provides an outline of the important role of miRNAs in controlling different mitochondrial activities.

Journal of Cellular Biochemistry

Inhibition of PI3K/Akt Signaling Alters Expression of Regulators

1122

Nyam-Osor Chimge, Aleksandr V. Makeyev, Sabine J. Waigel, Badam Enkhmandakh, and Dashzeveg Bayarsaihan

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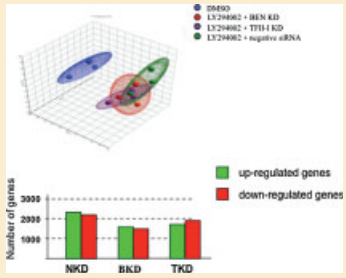
The PI3K/Akt signaling pathway is critical in maintaining the pluripotency of mouse embryonic stem cells (mESC). Activation of PI3K/Akt results in down-regulation of *Gtf2i* and *Gtf2ird1* encoding TFII-I family transcription factors. Human *GTF2I* and *GTF2IRD1* genes are prime candidates in Williams-Beuren syndrome, a complex neurodevelopmental disorder associated with cognitive, visuospatial, craniofacial and skeletal defects. To investigate how these genes might be involved in the process of cell differentiation, we performed microarray profiling of mESC upon inhibition of PI3K/Akt signaling. This analysis revealed significantly altered expression of developmentally important regulators. Genome-wide promoter ChIP-chip mapping revealed that the majority of differentially expressed genes are direct TFII-I targets. The data support the hypothesis that upregulation of TFII-I factors leads to activation of a specific group of developmental genes during mESC differentiation.



Effects of Tat in MSC Survival and Differentiation

1132

Davide Gibellini, Anna Miserocchi, Pier Luigi Tazzari, Francesca Ricci, Alberto Clò, Silvia Morini, Cristina Ponti, Gianandrea Pasquinelli, Isabella Bon, Pasqualepaolo Pagliaro, Marco Borderi, and Maria Carla Re

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In addition to immune system impairment, several clinical studies have indicated that HIV replication is correlated with a progressive derangement of central nervous system, bone, fat tissue, kidney and cardiovascular system. Since HIV infection is an independent risk factor for atherosclerosis development and cardiovascular damage, Gibellini and coworkers analysed the effects of Tat protein, a key factor in HIV replication and pathogenesis, in vessel-wall derived MSC survival and differentiation. High concentrations of Tat induced apoptosis activation in subconfluent MSCs suggesting that the Tat-related survival impairment of MSCs could be effective when high degree of HIV replication levels occurred, as in naïve patients. Tat is also able to affect MSC differentiation to adipogenesis and endotheliogenesis. Tat enhanced the adipogenesis differentiation of MSCs by the transcription and activity upregulation of PPARγ. Conversely, Tat inhibited the differentiation of MSCs to endothelial cells by downregulating the expression of VEGF-induced endothelial markers. These data indicated that the Tat-induced derangement of MSCs' survival and differentiation could play an important role in promoting vascular damage and atherosclerosis in the course of HIV disease.