Molecular Cancer Research

Highlights

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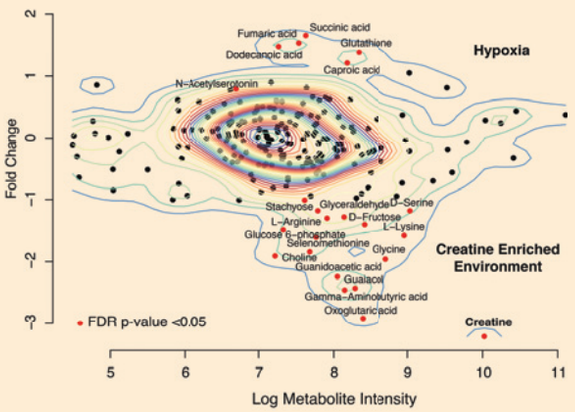
Selected Articles from This Issue



Metabolic Reprogramming Drives Tumor Heterogeneity

Heiland *et al.* **Page 655**

The heterogeneity of glioma is thought to underlie their limited response to therapy and poor prognosis. The transcriptional heterogeneity was found to be driven by metabolic reprogramming and microenvironmental influences. In particular, creatine maintained a reduction of reactive oxygen species (ROS) within the tumor leading to an inhibition of HIF-signaling. These effects shifted the transcriptional pattern toward a proneural subtype and reduced the rate of tumor migration and invasion *in vitro*. Combined, this study uncovers a regulatory function of the tumor microenvironment (TME) by metabolic-driven, transcriptional reprogramming in infiltrating glioma cells.

Distinct and Opposing Functions of BRD2 and BRD4 in EMT

Andrieu *et al.* **Page 580**

The initiation and progression of cancer is often a complex process due to genetic and epigenetic alterations. Recently, a family of transcription factors known as bromodomain and extraterminal (BET) domain proteins have been shown to be important regulators of cancer progression and have been targeted in many cancers. The current Rapid Impact article, by Andrieu and Denis, manipulates individual BET proteins to reveal independent transcriptional programs in the context of epithelial-to-mesenchymal transition (EMT) in breast cancer model systems. Importantly, these results suggest that epigenetic plasticity invoked by various BET proteins should be considered when designing targeted epigenetic therapies.

lncRNA MANCR Regulates Cell Proliferation and Survival

Tracy *et al.* **Page 587**

Long non-coding RNAs (lncRNAs) are increasingly demonstrated to be important regulators in cancer, serve as biomarkers of prognosis, and become potential therapeutic targets. However, the molecular functions of most lncRNAs remain poorly understood. Here, Tracy and colleagues functionally characterize a novel lncRNA, MANCR, which is upregulated in aggressive breast cancer. Knockdown studies reveal essential roles for MANCR in supporting cell cycle, cell viability, and genomic integrity. Importantly, the greater frequencies of defective cytokinesis and cell death observed upon MANCR depletion indicate MANCR as a potential target in breast cancer therapy.

Contribution of the miR-888 Cluster in Prostate Cancer

Hasegawa *et al.* **Page 669**

Prostate cancer is the second leading cause of male cancer-related death in the U.S. Here, the miR-888 cluster (composed of seven human miRNAs) is identified as a novel non-coding RNA network elevated in expressed prostatic secretion (EPS) urine from high-grade prostate cancer patients. Assessment using *in vitro* approaches revealed that the miR-888 cluster modulates prostate cancer progression, i.e. proliferation, migration, invasion, colony formation. miR-888 and miR-891a were validated as oncogenes and accelerated tumor growth in mice. This work provides new insight into molecular mechanisms for aggressive prostate cancer and indicates cluster members as promising diagnostic and therapeutic tools. Moreover, dysregulation of cluster members in other cancers suggests wider clinical implications.

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