Molecular Cancer Research

Highlights

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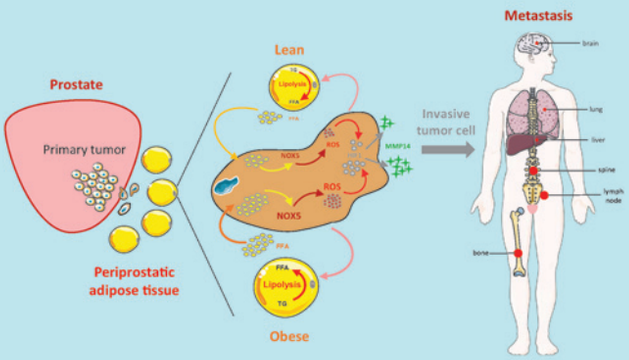
Selected Articles from This Issue



Lipids from Adipocytes Support Prostate Cancer Progression

Laurent *et al.* Page 821

Adipose tissue induces a pro-tumorigenic effect and promotes cancer aggressiveness. Here, Laurent and colleagues demonstrate that periprostatic adipose tissue (PPAT) engages in bidirectional interactions with prostate cancer cells, which are up-regulated by obesity. Prostate cancer cells induced lipolysis in adipocytes, thereby releasing free fatty acids (FFAs) into the microenvironment. FFA uptake by prostate cancer cells increased both expression of the NADPH oxidase NOX5 and intracellular levels of reactive oxygen species (ROS). This in turn led to increased activity of the HIF1/MMP14 pathway and tumor invasion. Analysis of prostate tumor sections revealed that cells at the invasive front harbor increased NOX5 and MMP14 expression when adjacent to PPAT, thus underscoring the importance of these observations.

ALK Fusions in LMS

Davis *et al.* Page 676

Leiomyosarcoma is an aggressive soft tissue tumor that responds poorly to systemic chemotherapy, and for which no targeted molecular therapies are currently available. Here, Davis and colleagues describe the first functional validation of recurrent gene fusions with ALK kinase, a targetable oncogene with therapeutic potential. Cells bearing these fusions were shown to be highly sensitive to kinase inhibitors such as lorlatinib. These findings suggest that clinical cases of sarcoma, particularly leiomyosarcoma, could harbor undiscovered driver gene fusions that may significantly improve clinical outcomes.

NF-κB and PARP1 Form a Loop Regulating DNA Repair

Li *et al.* Page 761

DNA-damaging chemotherapy is a standard intervention for acute myeloid leukemia (AML), but acquired resistance to these therapies via activation of NF-κB is a major clinical hurdle. Here, Li and colleagues demonstrate that the NF-κB subunit RELA directly binds and regulates PARP1, a key mediator of the DNA damage response. Further, ablation of PARP1 was shown to inhibit NF-κB activity, and co-targeting of NF-κB and PARP1 with small molecules yielded robust responses *in vivo*. Taken together, this study sets forth a rationale for new clinical approaches to managing resistance to chemotherapy in AML.

Fusion and Stemness of Prostate Cancer Cells

Uygur *et al.* Page 806

Interactions between malignant and non-malignant cells in the tumor microenvironment have a significant bearing on the development, progression, and aggressiveness of cancer. In this study, Uygur and colleagues describe a novel interaction between prostate cancer cells and the normal muscle cells that surround the prostate gland. Contact between prostate cancer and muscle cells had pronounced effects on tumor cell biology, including upregulation of anti-inflammatory interleukins and subsequent expression of syncytin 1 and annexin A5, proteins involved in cancer cell fusion. Expression of these factors was shown to correlate with tumor stage, suggesting that tumor-muscle cell interactions may promote disease progression in clinical prostate cancer.