Molecular Cancer Research

Highlights

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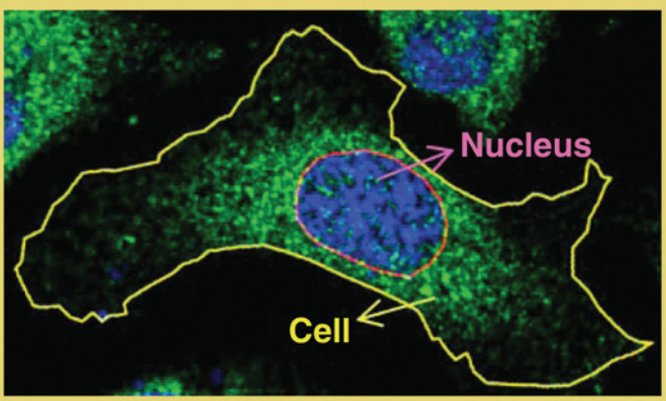
Selected Articles from This Issue



BRCA1 Activates HO-1 Transcription

Labanca *et al.*_____Page 1455

Accumulation of reactive oxygen species (ROS) causes injury to cell structures, ultimately leading to cancer development. The antioxidant enzyme heme oxygenase 1 (HMOX1/HO-1) is responsible for the maintenance of the cellular homeostasis, playing a critical role in the oxidative stress and the regulation of prostate cancer (PCa) development and progression. Labanca and colleagues demonstrate that activation of BRCA1-NRF2/HO-1 axis defines a new molecular mechanism for the maintenance of the cellular homeostasis in PCa.

PARP Trapping: Impact on *In Vivo* Activity of PARP Inhibitors

Hopkins *et al.*_____Page 1465

Recent evidence indicates that the cytotoxicity of PARP inhibitors is due in part to trapping of PARP onto single-strand breaks. It has been proposed that a subset of PARP inhibitors trap allosterically; however, direct evidence of this has not been reported. The study by Hopkins and colleagues reveals that trapping is not allosteric and is instead due to catalytic inhibition. Additionally, trapping is associated with reduced tolerability *in vivo*, and PARP inhibitors spanning a broad range of trapping potency elicit comparable efficacy at MTD in xenograft models. These results have implications for the suitability of different PARP inhibitors for inclusion in different combination regimens.

IL6 Mediates Crosstalk Between Immune and Cancer Cells

Patel *et al.*_____Page 1502

The tumor microenvironment (TME) is involved in promoting tumor survival and progression. The current study investigates intercellular communication within the TME between colorectal cancer and immune cells using *in vitro* co-culture systems. Interestingly, immune cell IL6 secretion promotes cancer cell invasion and release of miR-21 and miR-29b, which stimulates further IL6 production by surrounding immune cells. These findings offer a deeper understanding of how cells communicate within the TME and demonstrate that miRNAs are important mediators of this process. Identifying these key signals is crucial for the development of novel therapies targeting the TME.

Calcipotriol Targets LRP6

Arensman *et al.*_____Page 1509

The tumor suppressive actions proposed for vitamin D include its capacity to inhibit Wnt signaling. Identifying a subset of vitamin D receptor (VDR)-expressing pancreatic cancer cells responsive to calcipotriol, a vitamin D analog, Arensman and coworkers describe a novel biochemical mechanism through which vitamin D inhibits Wnt signaling. Calcipotriol increased LDLR-adaptor protein 1 (LDLRAP1) expression resulting in rapid reduction in protein levels of LDLR-related protein 6 (LRP6), a requisite co-receptor for canonical Wnt signaling. Inhibition of Wnt signaling decreased VDR expression; thus, revealing a reciprocal feedback loop between Wnt and vitamin D signaling. In summary, calcipotriol or other vitamin D analogs may be particularly efficacious against tumors with intact VDR and Wnt signaling activity.