Molecular Cancer Research Highlights

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Selected Articles from This Issue

Telomerase Expression in Tumor Adjacent Breast Tissue

Trujillo *et al.* _____**Page 1209**

In this study, Trujillo and coworkers show that the field of histologically normal tissue up to 1 centimeter from human breast tumors contains a population of epithelial cells with telomerase levels similar to the patient-matched tumor. This population has a mechanism for limitless replicative capacity and exists within tissue that has previously been shown to exhibit genomic instability and a microenvironment that supports tumor initiation. Because adequate surgical margins are often no more than a few millimeters from the tumor margin, in many cases, this tissue is not removed during breast-conserving surgery and may have implications in local recurrence rates.

Activation of Pro-MSP by Hepsin

Ganesan *et al.* _____**Page 1175**

The transmembrane serine protease hepsin is a highly upregulated gene in prostate cancer that promotes tumor progression and metastasis in preclinical models. Based on its substrate profile, Ganesan and colleagues investigated whether hepsin activates the precursor form of the plasminogen-like growth factor macrophage-stimulating protein (MSP). They show that both soluble and cell surface–expressed hepsin efficiently convert the inactive zymogen-like MSP precursor into a functionally competent heterodimeric form that induces phosphorylation of its cognate receptor RON and downstream signaling proteins promoting epithelial cell motility. These findings suggest that hepsin regulates the MSP/RON signaling pathway in cancer, immune disorders, and tissue homeostasis.

FIP200 in DNA Damage Repair and Cell Survival

Bae and Guan _____**Page 1232**

FIP200 is a component of the ULK1/Atg13/FIP200 complex essential for autophagy induction in mammalian cells, which has been previously implicated in breast cancer. It is not clear, however, how autophagy function of FIP200 may contribute to its role in breast or other cancers. Here, Bae and Guan present data suggesting a novel function for FIP200 in the regulation of DNA damage response and cell survival through its activity in autophagy. These results suggest the possibility of FIP200 or other autophagy proteins as a potential treatment to enhance the efficiency of cancer therapy using DNA damage–inducing agents.

Deregulation of mTORC1 in ccRCC

Kucejova *et al.* _____**Page 1255**

To adapt to unfavorable growth conditions such as hypoxia, mTORC1, a critical regulator of cell growth, is inactivated. mTORC1 inhibition by hypoxia is mediated by REDD1, a HIF target gene. As a consequence of VHL inactivation, HIF and hypoxia-inducible genes are constitutively upregulated in clear-cell renal cell carcinoma (ccRCC), but whether this leads to REDD1 upregulation is unclear and mTORC1 is commonly activated in ccRCC. Kucejova and colleagues show that REDD1 is consistently upregulated in ccRCC and that, whereas in some tumors REDD1 is engaged in mTORC1 inhibition, in others, strategies have evolved to uncouple mTORC1 from REDD1. Specifically, Kucejova and colleagues found somatic mutations in REDD1 and TSC1, which is required for mTORC1 inhibition by REDD1.

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