Molecular Cancer Research

Highlights

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Selected Articles from This Issue

EGFR Mutations in Neuroblastoma

Keller *et al.* Page 740

Neuroblastoma is an aggressive childhood cancer. Current treatment for this disease is associated with many side effects. Thus, there is an urgent need to develop targeted therapy for this cancer. In this study, it is discovered for the first time that neuroblastomas express a novel EGFR extracellular domain deletion mutant, EGFRΔ768. Further characterization of the EGFRΔ768 revealed that it possessed distinct pro-oncogenic properties which were different from both the EGFRvIII mutant and the wild type receptor. These findings provide new insight and reignite an interest in EGFR targeting therapy for neuroblastoma. There is also therapeutic implication for other tumors expressing this novel mutant.

AMPK Causes G1 Arrest in LKB1-null Cells by CAMKK2 Pathway

Fogarty *et al.* Page 683

The gene encoding the tumor suppressor LKB1, an upstream kinase required for phosphorylation and activation of AMP-activated protein kinase (AMPK) and twelve AMPK-related kinases (ARKs), is mutated or deleted in many cancers. Fogarty and colleagues report that increasing cytosolic Ca^{2+}, which activates AMPK (but not the ARKs) via the alternate upstream kinase CaMKK2, causes a cell cycle arrest in LKB1-null tumor cells that is AMPK-dependent. This suggests that the rapid proliferation of these cells is due to their low activity of AMPK rather than the ARKs, and also suggests a novel approach (CaMKK2 activation) to inhibit growth of LKB1-deficient tumors.

Role of the AHR in Oral Cancer Migration and Tumorigenesis

Stanford *et al.* Page 696

This study investigates the role of an environmental carcinogen sensor, the aryl hydrocarbon receptor (AHR), in oral squamous cell carcinoma (OSCC). The significance of the work lies in the connection between environmental chemicals and oral cancer, the understanding of the basic signaling pathways in OSCC, and the potential for the oral microbiome to influence OSCC through the AHR. The data suggests that common environmental and bacterial-derived AHR ligands play an important role in development and progression of OSCC, and specifically in development of cancer stem-like cells. The work implicates a novel mechanism of OSCC progression and supports targeting the AHR for treatment of OSCC and other carcinomas.

GR and ER Increase Expression of Differentiation Genes

West *et al.* Page 707

It has been previously recognized that glucocorticoids inhibit estrogen-mediated ER^+ breast cancer cell proliferation. West and colleagues now report that patients with early-stage ER^+ breast cancers expressing high glucocorticoid receptor (ER^+/GR-high tumors) have improved relapse-free survival compared to patients with ER^+/GR-low disease. Furthermore, ER^+ cell line models reveal that ER and GR co-localize to regulatory regions of differentiation genes (e.g., IGFBP4, KDM4B, and VDR) and subsequently demonstrate increased gene expression. In patient samples, expression of IGFBP4, KDM4B, or VDR correlates with improved prognosis. The results suggest that ER and GR genomic cooperativity contributes to ER^+ breast cancer biology and patient outcome.

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