Molecular Cancer Research **Highlights**

March 2014 • Volume 12 • Number 3

Selected Articles from This Issue

Role of Espin in Melanoma

Yanagishita *et al.* **Page 440**

Espin (ESPN) is a multifunctional actin-bundling protein and is an important regulator of cytoskeleton dynamics. At present, there have been no reports showing the expression and function of Espin in cancers, including melanoma. Yanagishita and colleagues reveal that Espin is strongly expressed in human melanomas as well as in *RET*-transgenic mice. Moreover, depletion of Espin has a dramatic impact on the metastatic activity of melanoma cells *in vitro* and *in vivo*. These findings reveal Espin not only as a novel metastatic regulator in melanoma but also as a potential biomarker for disease progression.

p63 Expression Is Regulated by RBM24 through mRNA Stability

Xu *et al.* **Page 359**

The p53 tumor suppressor family member, p63 (TP63), plays a pivotal role in epidermal development, aging, and tumorigenesis. In an effort to understand the underlying mechanism by which p63 expression is controlled, Xu and colleagues identify the RNA-binding protein RBM24 as a novel regulator of p63 status via mRNA stability. Specifically, overexpression of RBM24 decreases, whereas knockdown of RBM24 increases, p63 expression. Mechanistically, RBM24 is able to bind to multiple regions in the 3′UTR of p63 and destabilize the p63 transcript. Together, these observations provide significant insight into the understanding of how p63 expression is regulated through a posttranscriptional mechanism.

Triapine Disrupts Homologous Recombination Repair in EOC

Lin *et al.* **Page 381**

Management of epithelial ovarian cancer (EOC) that harbors wild-type BRCA remains a major challenge due to acquired chemoresistance and poor overall survival. Development of mechanism-based and/or targeted combination therapy approaches is critically needed for improved clinical outcome. Lin and colleagues demonstrate that triapine, a small molecule inhibitor of ribonucleotide reductase, sensitizes BRCA wild-type EOC cells to PARP and topoisomerase II inhibitors. Mechanistic studies demonstrate that triapine impairs homologous recombination repair (HRR) by obliterating CtIP phosphorylation, DNA double-strand break (DSB) resection, BRCA1 and Rad51 foci formation, and endonuclease-induced DSB repair. These findings provide a strong rationale for targeting HRR and using triapine to augment the efficacy of PARP and topoisomerase inhibitors for the treatment of BRCA wild-type EOC.

NF-κB Activation Underlies Anti-HER2 Resistance

Bailey *et al.* **Page 408**

HER2/Neu (ERBB2) is a tyrosine kinase and is a major contributor to disease progression in various types of breast cancer. Consequently, its biomarker status is fundamentally important and its activity is a key target for therapeutics. Despite initial efficacy, HER2-targeted treatment approaches eventually result in resistance. Here, Bailey and colleagues report that NF-κB activity renders HER2-positive cancers resistant to HER2-directed therapy. Interestingly, Lapatinib-resistant cells had altered NF-κB and were more sensitive to simultaneous HER2 and NF-κB inhibitor treatment than either therapy alone. Through the use of genomic analyses, a NF-κB signature was deduced that correlated with clinical outcome. Thus, this study implicates NF-κB in HER2 therapy resistance and suggests that combinatorial NF-κB and HER2 inhibition has therapeutic benefit.

Downloaded from mcr.aacrjournals.org on October 22, 2021. © 2014 American Association for Cancer Research.

AACR American Association for Cancer Research

Molecular Cancer Research

Highlights of This Issue

Mol Cancer Res 2014;12:295.

Updated version Access the most recent version of this article at:
http://mcr.aacrjournals.org/content/12/3/295

E-mail alerts Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions To request permission to re-use all or part of this article, use this link
http://mcr.aacrjournals.org/content/12/3/295.
Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.

Downloaded from mcr.aacrjournals.org on October 22, 2021. © 2014 American Association for Cancer Research.