Activity of Edelfosine against MCL and CLL

Mollinedo et al. ________Page 2046

There is a need for additional therapeutic options with activity against mantle cell lymphoma (MCL) and chronic lymphocytic leukemia (CLL). In this issue, Mollinedo and colleagues found that the alkyl-lysophospholipid analog edelfosine could induce apoptosis in MCL and CLL cell lines and patient-derived cells, while sparing normal cells. Edelfosine-induced apoptosis was mediated by colustering of Fas/CD95 death receptor and lipid rafts. Further, edelfosine oral administration showed strong in vivo anti-MCL and anti-CLL activity in xenograft mouse models. These data show a selective action of edelfosine against tumor cells and support development of edelfosine as a therapy in MCL and CLL.

Decreased SELENBP1 in Esophageal Cancer

Silvers et al. ___________Page 2009

Although decreased serum selenium levels have been associated with a number of malignancies, further work is needed to clinically demonstrate the benefits of selenium supplementation, as well as to define the mediators of these potential benefits. Here, Silvers and colleagues demonstrate that selenium-binding protein 1 (SELENBP1) expression is decreased in patients with esophageal adenocarcinoma, and that its expression is modulated by both epigenetic and posttranscriptional mechanisms. Further, ectopic overexpression of SELENBP1 in esophageal adenocarcinoma cell lines resulted in enhanced apoptosis, increased senescence, and greater sensitivity to cisplatin. These findings may impact strategies for the chemoprevention and/or treatment of esophageal cancer.

FBXW7 and MYCN Mutations in Wilms’ Tumor

Williams et al. ___________Page 2036

Wilms’ tumor (WT) has been associated with WT1, CTNNB1, WTX, and TP53 mutations, but these mutations are not detected in the majority of WT cases. Williams and colleagues used SNP arrays and sequencing to identify FBXW7 as a novel Wilms’ tumor gene. FBXW7 was deleted or mutated in about 4% of tumors examined, and FBXW7 aberrations were associated with epithelial-type histology, a subtype with no previously defined molecular markers. Additionally, the authors found that MYCN gain was strongly associated with diffuse anaplastic WT. As FBXW7 mediates MYCN degradation, these results suggest that elements of a common pathway are deregulated in different WT subtypes.

Induction of Steroid Receptor Coactivators by Tamoxifen

Haugan Moi et al. ________Page 2176

The steroid receptor coactivator SRC-3/AIB1 is overexpressed in breast cancers and is associated with reduced sensitivity to endocrine treatment, especially when overexpressed with HER-2/neu. In this issue, Haugan Moi and colleagues studied breast cancer specimens from a clinical trial and found that tamoxifen in the 1–20 mg dose range induced a significant upregulation of SRC-3/AIB1 mRNA. The authors found that levels of SRC-3/AIB1 and HER-2/neu mRNA were correlated, and low SRC-3/AIB1 levels were associated with improved disease-free survival. These findings suggest that the oncogene SRC-3/AIB1 is an important mediator of tamoxifen agonistic effects.
Clinical Cancer Research

Highlights of This Issue


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