Clinical Cancer Research **Highlights**

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Selected Articles from This Issue

MiRNA Profiling of Sporadic and Hereditary Medullary Thyroid Cancer

Abraham *et al.* Page 4772

MicroRNAs are increasingly important prognostic markers in cancer, but have not been well characterized in medullary thyroid cancer (MTC). Abraham and colleagues performed miRNA microarray profiling on 45 tumors and correlated findings with clinical outcomes. MiRs-183 and 375 were overexpressed and miR-9* was underexpressed in sporadic versus hereditary MTC. MiR-183 and 375 overexpression predicted residual disease, distant metastases, and mortality. MiR-183 knockdown *in vitro* reduced cellular proliferation in association with an increase in LC3B, suggesting cell death via autophagy. These results show that miRNAs have potential as prognostic biomarkers and therapeutic targets in MTC.

Role of MiR-146a in NK/T Cell Lymphoma

Paik *et al.* Page 4761

Several pathogenic mechanisms of EBV-associated extranodal NK/T cell lymphoma (NKTL) have been suggested, including microRNA-medicated oncogenesis. In this study, Paik and colleagues investigated the role of miR-146a in NKTL. Using human tissues and cell lines, they found that miR-146a functioned as a tumor suppressor, through downregulation of the TNF receptor–associated factor-6 (TRAF6)/NFκB pathway. The expression level of miR-146a was also found to have prognostic significance in NKTL. These observations provide new insight into the pathogenesis of NKTL and suggest that miR-146a is a useful prognostic factor and a potential therapeutic target in this disease.

FES PET Measures Endocrine Therapy Pharmacodynamics

Linden *et al.* Page 4799

In vivo monitoring of regional estrogen binding to tumor estrogen receptor (ER) in metastatic breast cancer is feasible using ^{18}F-fluoroestradiol positron emission tomography (FES PET). To determine whether estrogen-depleting strategies, such as aromatase inhibitors, impact ER-estradiol binding differently than ER-blocking strategies, such as tamoxifen or fulvestrant, Linden and colleagues analyzed serial quantitative FES PET in patients enrolled in experimental imaging studies. Unlike aromatase inhibitors, ER-blocking therapies blocked ER uptake effectively at tumor and uterine sites. However, tamoxifen more completely blocked uptake than fulvestrant, consistent with recent clinical reports suggesting increased efficacy for higher fulvestrant doses.

PK/PD Relationships of Erlotinib in Adults and Children

White-Koning *et al.* Page 4862

Clinical trials in pediatrics are often conducted after treatments have been approved for adult use, but data are infrequently combined between pediatric and adult studies. By using a population pharmacokinetic approach to simultaneously analyze data from two clinical trials (a neoadjuvant pilot study in adults and a phase 1 study in pediatrics), White-Koning and colleagues show that the difference in recommended erlotinib dose between pediatric and adult patients is related to pharmacokinetic particularities and not to pharmacodynamic specificities. These results are useful not only for the clinical use of erlotinib, but also to encourage future analysis of combined data from children and adults.