Cancer Research Highlights

Selected Articles from this Issue AUGUST 1, 2004

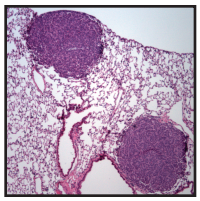
PI3K-Related Kinase Linked to Brain Tumors

Broderick *et al.* **Page 5048**

The phosphatidylinositol 3-kinases (PI3Ks) are involved in signaling pathways that are deregulated in tumorigenesis. To determine if PI3Ks are genetically altered in brain tumor development, Broderick *et al.* performed a mutational study of a specific catalytic subunit of the PI3K family, *PIK3CA*. Their analyses identified alterations of *PIK3CA* in a significant fraction of anaplastic oligodendrogliomas, high-grade astrocytomas, glioblastomas and medulloblastomas. These findings implicate *PIK3CA* as an oncogene in a wide spectrum of adult and pediatric brain tumors, and suggest an important role as a diagnostic marker or a therapeutic target in these cancers.

Yeast-Based Immunotherapy Targets, Ablates Ras-Mutant Tumors

Lu *et al.* **Page 5084**



DNA mutations caused by chemical exposure can lead to unregulated cell proliferation and carcinogenesis. Urethane exposure in mice triggers single amino acid mutations in the Ras oncoprotein that result in lung hyperplasias, adenomas, and adenocarcinomas. Lu *et al.* show that therapeutic administration of whole recombinant *S. cerevisiae* heterologously expressing mammalian mutant Ras protein resulted in complete regression of established, mutant Ras-bearing lung tumors in the urethane-exposed A/J mice. Coupled with tumor genotyping for mutations in Ras oncogenes, the yeast-based immunotherapeutic approach will be applied to treat Ras mutation-bearing human cancers.

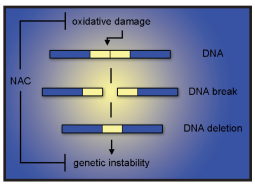
Podocalyxin Expression Predicts Breast Cancer Progression

Somasiri *et al.* **Page 5068**

In ductal breast carcinomas, metastatic progression is often preceded by a general perturbation of cell junctions that does not necessarily rely upon E-cadherin suppression. Somasiri *et al.* demonstrate that forced expression of the anti-adhesive cell surface molecule podocalyxin initiates just such a junctional perturbation in breast carcinoma cells. Using tissue microarray technology, the authors also found that podocalyxin is overexpressed in a distinct subset of invasive breast tumors linked to poor outcome. Therefore, podocalyxin is a prognostically significant independent marker of breast cancer progression that may also play a functional role in the process.

Antioxidant Counters AT-Manifested DNA Damage

Reliene *et al.* **Page 5148**



Ataxia telangiectasia (AT) is a cancer-prone human disorder associated with oxidative stress and genetic instability, which are implicated in carcinogenesis. To investigate the role of antioxidant intake on genetic instability in AT, Reliene *et al.*, treated ATM-deficient mice with N-acetyl-cysteine (NAC) during embryonic development. Untreated ATM-deficient mice displayed elevated levels of oxidative DNA damage deletions. NAC-treatment reduced oxidative DNA damage and deletions to the wild-type level. Therefore, antioxidants counteracting genetic instability might reduce cancer risk in ATM deficiency.