New Roles Opined for OPCML. ..................... 115
S.Y. Wu and A.K. Sood
Commentary on McKie et al., p. 156

Prospective
Cancers of the Colon and Rectum: Identical or Fraternal Twins? .................. 117
T.S. Hong, J.W. Clark, and K.M. Haigis

Identification of Human Regulatory T Cells in the Setting of T-Cell Activation and Anti–CTLA-4 Immunotherapy on the Basis of Expression of Latency-Associated Peptide. .... 122
J. Sun, D.N. Tong, T. Fu, and P. Sharma

Précis: Latency-associated peptide is an accurate surrogate marker of regulatory T cells that will facilitate functional studies of immunotherapy.

Inherited Variation at Chromosome 12p13.33, Including RAD52, Influences the Risk of Squamous Cell Lung Carcinoma .................. 131

Précis: A pathway-based analysis of a genome-wide association study identifies a squamous cell lung carcinoma susceptibility locus harboring the RAD52 gene.

In The Spotlight

Another LAP in the Race........... 107
S.M. Lee and C. Yee
Commentary on Sun et al., p. 122

New Lung Cancer Susceptibility Locus Identified: Significance and Implications for Other Genome-Wide Association Studies .......... 110
T.A. Sellers and Y.A. Chen
Commentary on Shi et al., p. 131

Regulating the TRAIL of Destruction: How A20 Protects Glioblastomas from TRAIL-Mediated Death........... 112
I. Verbrugge and R.W. Johnstone
Commentary on Bellail et al., p. 140

SELECTED HIGHLIGHTS OF RESEARCH BRIEFS
A20 Ubiquitin Ligase–Mediated Polyubiquitination of RIP1 Inhibits Caspase-8 Cleavage and TRAIL-Induced Apoptosis in Glioblastoma ................. 140

Précis: Overexpression of the ubiquitin ligase A20 is a mechanism of resistance to TRAIL pathway–targeted therapy in glioblastoma.

The OPCML Tumor Suppressor Functions as a Cell Surface Repressor–Adaptor, Negatively Regulating Receptor Tyrosine Kinases in Epithelial Ovarian Cancer .... 156

Précis: OPCML binds the extracellular domains of specific receptor tyrosine kinases to induce their endocytic internalization and proteasomal degradation.

Essential Gene Profiles in Breast, Pancreatic, and Ovarian Cancer Cells ....... 172

Précis: Analysis of a large-scale shRNA dropout screen with a new scoring metric facilitates the identification of essential genes and putative oncogenic drivers.

Correction
Correction: An LXR Agonist Promotes Glioblastoma Cell Death through Inhibition of an EGFR/AKT/SREBP-1/LDLR-Dependent Pathway ............... 190

For more News and Research Watch, visit Cancer Discovery online at www.AACR.org/CDnews. Online-only News stories include the following:

- NCATS Is Out of the Bag
- Putting Tumors to the Blood Test
- Immune Cells May Promote Skin Cancer
- Web Applications Aid Clinical Trial Recruitment

ON THE COVER

McKie and colleagues show that OPCML expression is silenced in multiple tumor types, including the vast majority of high-grade serous ovarian tumors, and correlates with poor prognosis. They further establish an extracellular mechanism of OPCML-mediated tumor suppression through negative regulation of a specific group of receptor tyrosine kinases (RTK). Through binding to RTK extracellular domains, OPCML induces RTK membrane redistribution, internalization, and degradation. Recombinant OPCML downregulated the same RTKs in vivo and inhibited ovarian cancer cell growth, suggesting that extracellular protein therapy may be useful in the treatment of OPCML-deficient tumors. For details, please see the article by McKie and colleagues on page 156.