# Table of Contents

## HISTORICAL PERSPECTIVE

1. Fifty Years of Tobacco Carcinogenesis Research: From Mechanisms to Early Detection and Prevention of Lung Cancer  
   Stephen S. Hecht and Eva Szabo

## COMMENTARY

9. Physical Activity and Gastric Cancer: So What? An Epidemiologist’s Confession  
   Tim Byers  
   See article, p. 12

## RESEARCH ARTICLES

12. Physical Activity Is Associated with Reduced Risk of Gastric Cancer: A Systematic Review and Meta-analysis  
   Siddharth Singh, Jithinraj Edakkanambeth Varayil, Swapna Devanna, Mohammad Hassan Murad, and Prasad G. Iyer  
   See commentary, p. 9

   Susan R. Mallery, Meng Tong, Gregory C. Michaels, Amber R. Kiyani, and Stephen S. Hecht

33. Regular Aspirin Use and Risk of Multiple Myeloma: A Prospective Analysis in the Health Professionals Follow-up Study and Nurses’ Health Study  
   Brenda M. Birmann, Edward L. Giovannucci, Bernard A. Rosner, and Graham A. Colditz

42. Nutrition and Physical Activity Cancer Prevention Guidelines, Cancer Risk, and Mortality in the Women’s Health Initiative  
   Cynthia A. Thomson, Marjorie L. McCullough, Betsy C. Wertheim, Rowan T. Chlebowski, Maria Elena Martinez, Marcia L. Stefanick, Thomas E. Rohan, JoAnn E. Manson, Hilary A. Tindle, Judith Ockene, Mara Z. Vitolins, Jean Wactawski-Wende, Gloria E. Sarto, Dorothy S. Lane, and Marian L. Neuhausser

54. Metformin Inhibits Skin Tumor Promotion in Overweight and Obese Mice  
   L. Allyson Checkley, Okiyung Rho, Joe M. Angel, Jiyoung Cho, Jorge Blando, Linda Beltran, Stephen D. Hursting, and John DiGiovanni

65. Luteolin Nanoparticle in Chemoprevention: In Vitro and In Vivo Anticancer Activity  

74. A Derivative of Chrysins Suppresses Two-Stage Skin Carcinogenesis by Inhibiting Mitogen- and Stress-Activated Kinase  
   Haidan Liu, Joonsoong Hwang, Wei Li, Tae Woong Choi, Kangdong Liu, Zunnan Huang, Jae-Hyuk Jang, N.R. Thimmegowda, Ki Won Lee, In-Ja Ryoo, Jong-Seog Ahn, Ann M. Bode, Xinning Zhou, Yifeng Yang, Raymond L. Erikson, Bo-Yeon Kim, and Zigang Dong

86. Kava Blocks 4-(Methylnitrosamino)-1-(3-pyridyl)-1-Butanone–Induced Lung Tumorigenesis in Association with Reducing O6-methylguanine DNA Adduct in A/J Mice  

97. Effect of a Low-Fat Fish Oil Diet on Proinflammatory Eicosanoids and Cell-Cycle Progression Score in Men Undergoing Radical Prostatectomy  

105. Dynamic Tumor Growth Patterns in a Novel Murine Model of Colorectal Cancer  

114. Temporal and Spatial Evolution of Somatic Chromosomal Alterations: A Case-Cohort Study of Barrett’s Esophagus  
   Xiaohong Li, Patricia C. Calipeau, Thomas G. Paulson, Carissa A. Sanchez, Jessica Arnaudo, Karen Liu, Cassandra L. Saifer, Rumen L. Kostadinov, Robert D. Odze, Mary K. Kuhner, Carlo C. Maley, Steven G. Self, Thomas L. Vaughan, Patricia L. Blount, and Brian J. Reid
### Table of Contents

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>128</td>
<td>Folate Deficiency Induces Dysfunctional Long and Short Telomeres; Both States Are Associated with Hypomethylation and DNA Damage in Human WIL2-NS Cells</td>
<td>Caroline F. Bull, Graham Mayrhofer, Nathan J. O’Callaghan, Amy Y. Au, Hilda A. Pickett, Grace Kah Mun Low, Dimphy Zeegers, M. Prakash Hande, and Michael F. Fenech</td>
</tr>
<tr>
<td>139</td>
<td>Licochalcone A, a Natural Inhibitor of c-Jun N-Terminal Kinase 1</td>
<td>Ke Yao, Hanyong Chen, Mee-Hyun Lee, Haitao Li, Weiya Ma, Cong Peng, Nu Ry Song, Ki Won Lee, Ann M. Bode, Ziming Dong, and Zigang Dong</td>
</tr>
<tr>
<td>150</td>
<td>A Novel Molecular Pathway for Snail-Dependent, SPARC-Mediated Invasion in Non–Small Cell Lung Cancer Pathogenesis</td>
<td>Jeanette L. Grant, Michael C. Fishbein, Long-Sheng Hong, Kostyantyn Krysan, John D. Minna, Jerry W. Shay, Tonya C. Walser, and Steven M. Dubinett</td>
</tr>
<tr>
<td>161</td>
<td>Cognitive Factors Associated with Adherence to Oral Antiestrogen Therapy: Results from the Cognition in the Study of Tamoxifen and Raloxifene (Co-STAR) Study</td>
<td>Heidi D. Klepin, Ann M. Geiger, Hanna Bandos, Joseph P. Costantino, Stephen R. Rapp, Kaycee M. Sink, Julia A. Lawrence, Hal H. Atkinson, and Mark A. Espeland</td>
</tr>
<tr>
<td>169</td>
<td>eRapa Restores a Normal Life Span in a FAP Mouse Model</td>
<td>Paul Hasty, Carolina B. Livi, Sherry G. Dodds, Diane Jones, Randy Strong, Martin Javors, Kathleen E. Fischer, Lauren Sloane, Kruthi Munty, Gene Hubbard, Lishi Sun, Vincent Hurez, Tyler J. Curiel, and Zelton Dave Sharp</td>
</tr>
</tbody>
</table>

**ABOUT THE COVER**

In 2007, the International Agency for Cancer Research presented compelling evidence that linked smokeless tobacco use to the development of human oral cancer. While these findings imply vigorous local carcinogen metabolism, little is known regarding levels and distribution of Phase I, II, and drug egress enzymes in human oral mucosa. The current study integrated clinical data, imaging studies, and histopathologic analyses of an oral squamous cell carcinoma that arose at the site of smokeless tobacco quid placement. The cover depicts a three-dimensional iCAT image of the buccal aspect of the patients left mandibular body. The marked bone destruction associated with tobacco quid placement in the buccal vestibule adjacent to the patient’s second and first mandibular molars is readily apparent. Immunoblot and immunohistochemical (IHC) analyses were employed to identify tumor and normal human oral mucosal smokeless tobacco-associated metabolic bioactivation and detoxification enzymes. Human oral epithelium contains every known Phase I enzyme capable of nitrosamine oxidative bioactivation with ~2 fold interdonor differences in protein levels. IHC studies confirmed that oral mucosal nitrosamine metabolizing enzymes reside in the basal and suprabasilar regions, sites of ongoing keratinocyte DNA replication. Clearly, variations in product composition, capacity for nitrosamine oxidative metabolism and exposure duration will modulate clinical outcomes. The data presented here form a coherent picture consistent with the abundant experimental data that link tobacco-specific nitrosamines to human oral cancer. See article by Mallery and colleagues (beginning on page 23) for more information.