

## CANCER PREVENTION RESEARCH

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## REVIEW

- 285**    **Mitochondria as a Novel Target for Cancer Chemoprevention: Emergence of Mitochondrial-targeting Agents**  
Mofei Huang, Charles R. Myers, Yian Wang, and Ming You

## RESEARCH BRIEF

- 307**    **An Improved Murine Premalignant Squamous Cell Model: Tobacco Smoke Exposure Augments NTCU-Induced Murine Airway Dysplasia**  
Lori D. Dwyer-Nield, Debbie G. McArthur, Meredith A. Tennis, Daniel T. Merrick, and Robert L. Keith

## RESEARCH ARTICLES

- 313**    **Targeting of CD40 and PD-L1 Pathways Inhibits Progression of Oral Premalignant Lesions in a Carcinogen-induced Model of Oral Squamous Cell Carcinoma**  
Jose A. Monteiro de Oliveira Novaes, Taghreed Hirz, Irene Guijarro, Monique Nilsson, Marlese A. Piseigna, Alissa Poteete, Hampartsoum B. Barsoumian, Jared J. Fradette, Limo N. Chen, Don L. Gibbons, Xiangjun Tian, Jing Wang, Jeffrey N. Myers, Mark J. McArthur, Diana Bell, William N. William Jr, and John V. Heymach  
PD-1/PD-L1 pathway blockade, as well as activation of the CD40 pathway, were able to prevent OPL progression into invasive OSCC in a murine model. A distinct pattern of immune modulation was observed when either the CD40 or the PD-1/PD-L1 pathways were targeted.
- 325**    **Optimization of Erlotinib Plus Sulindac Dosing Regimens for Intestinal Cancer Prevention in an Apc-Mutant Model of Familial Adenomatous Polyposis (FAP)**  
Ahmet M. Ulsan, Praveen Rajendran, Wan Mohaiza Dashwood, Omer F. Yavuz, Sabeeta Kapoor, Trace A. Gustafson, Michelle I. Savage, Powel H. Brown, Shizuko Sei, Altaf Mohammed, Eduardo Vilar, and Roderick H. Dashwood  
This investigation concludes that switching from continuous to once-per-week erlotinib, given at one-quarter of the current therapeutic dose, will exert good efficacy with standard-of-care sulindac against adenomatous polyps in the colon and small intestine, with clinical relevance for patients with FAP before or after colectomy.

- 337**    **Diet-Associated Inflammation Modulates Inflammation and WNT Signaling in the Rectal Mucosa, and the Response to Supplementation with Dietary Fiber**  
Fiona C. Malcomson, Naomi D. Willis, Iain McCallum, Long Xie, Nitin Shivappa, Michael D. Wirth, James R. Hébert, Betül Kocaadam-Bozkurt, Aycil Özturan-Sirin, Seamus B. Kelly, D. Michael Bradburn, Nigel J. Belshaw, Ian T. Johnson, and John C. Mathers  
Our finding that more inflammatory dietary components may impact large bowel health through effects on a well-recognized pathway involved in cancer development will strengthen the evidence base for dietary advice to help prevent bowel cancer.

- 347**    **Association of IgG Glycosylation and Esophageal Precancerosis Beyond Inflammation**  
Zhiyuan Wu, Huiying Pan, Di Liu, Di Zhou, Lixin Tao, Jie Zhang, Xiaonan Wang, Youxin Wang, Wei Wang, and Xiuhua Guo  
IgG glycosylation profile is associated with esophageal precancerosis and specific IgG glycans involves in the early stage of esophageal cancer, which is independent of inflammation.

- 355**    **Clinical Evaluation of DNA Ploidy for the Triage of HPV-Positive Chinese Women During Cervical Cancer Screening**  
**AC** Wei Cang, Qing Li, Liying Gu, Zubei Hong, Yuan Hu, Wen Di, and Lihua Qiu  
Results from this study indicate that DNA ploidy analysis has good performance in early detection of high-grade precancerous and cancerous lesions of the cervix. This strategy could be used in the triage of HPV-positive women in cervical cancer screening.

- 363**    **Effect of Sequential Rounds of Cervical Cancer Screening on Management of HPV-positive Women: A 15-year Population-based Cohort Study from China**  
Xiao-Qian Xu, Remila Rezhake, Shang-Ying Hu, Feng Chen, Xun Zhang, Qin-Jing Pan, Wen-Hua Zhang, Jun-Fei Ma, You-Lin Qiao, Fang-Hui Zhao, and Margaret Cruickshank  
The study highlights the sustained effectiveness of mainstream HPV triage methods, such as cytology and genotyping, after sequential rounds of cervical screening. It also suggests that use of HPV persistence across rounds can improve management of HPV-positive women in cervical cancer screening.

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**373 Screening for Pancreatic Ductal Adenocarcinoma: Are We Asking the Impossible?**

Katharine E. Caldwell, Alexander P. Conway, and Chet W. Hammill

For patients with pancreatic cancer, early stage detection offers the greatest survival benefit. However, the incidence of pancreatic cancer and associated mortality of pancreatic resections make development of a screening test a difficult, if not impossible, challenge.

**383 Baseline Oral Microbiome and All-cancer Incidence in a Cohort of Nonsmoking Mexican American Women**

Xiaotao Zhang, Kristi L. Hoffman, Peng Wei, Kplola Y. Elhor Gbitto, Reji Joseph, Fangyu Li, Paul Scheet, Shine Chang, Joseph F. Petrosino, and Carrie R. Daniel

Mexican American women suffer a disproportionate burden of chronic health conditions that increase cancer risk. Few investigations of the microbiome, a key determinant of host health, have been conducted among this group. Oral microbiota profiles may provide early and accessible cancer biomarker data on invasive bacteria or community disruptions.

**393 Effects of Supplemental Calcium and Vitamin D on Circulating Biomarkers of Gut Barrier Function in Patients with Colon Adenoma: A Randomized Clinical Trial**

Kelly Vermandere, Roberd M. Bostick, Hao Q. Tran, Andrew T. Gewirtz, Elizabeth L. Barry, Robin E. Rutherford, March E. Seabrook, and Veronika Fedirko

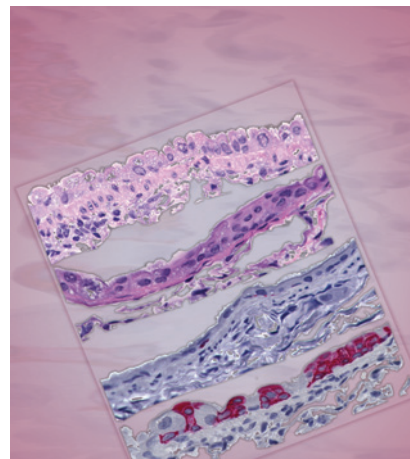
Calcium and vitamin D may be involved in regulating and maintaining the integrity of the intestinal mucosal barrier, the dysfunction of which results in exposure of the host to luminal bacteria, endotoxins, and antigens leading to potentially cancer-promoting endotoxemia and chronic colon inflammation. While our results suggest that daily supplementation with these chemopreventive agents does not modify circulating concentrations of gut permeability biomarkers, they support continued investigation of other potential modifiable factors, such as diet and excess adiposity, that could alter gut barrier function, to inform the development of treatable biomarkers of risk for colorectal neoplasms and effective colon cancer preventive strategies.

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## ABOUT THE COVER

Squamous cell lung cancer is a smoking-related malignancy characterized by the development of premalignant bronchial dysplastic lesions in the central airways. Reproducible preclinical models of squamous cell cancer have proven difficult to develop, and the most commonly employed model involves topical treatment with NTCU for up to 32 weeks. In a study beginning on page 307, Dwyer-Nield and colleagues report on an improved model where NTCU is combined with cigarette smoke exposure to induce more premalignant airway lesions in a shorter period of time (14 weeks). The cover shows H&E and cytokeratin 5-stained dysplastic airway lesions resulting from NTCU or NTCU + cigarette smoke exposure (40×). The lesions contain dysmorphic nuclei.



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