TABLE OF CONTENTS

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


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. Ulusan, 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. Malcolmson, Naomi D. Willis, Iain McCallum, Long Xie, Nitin Shivappa, Michael D. Wirth, James R. Hébert, Betul Kocaadam-Bozkurt, Ayçıl Özturan-Sirin, Seamus R. 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 Precarcinosis Beyond Inflammation

Zhiyuan Wu, Huaying Pan, Di Liu, Di Zhou, Lixin Tao, Jie Zhang, Xiaonian 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

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.
TABLE OF CONTENTS

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.

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.

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.