

Selected Publications by the UGI Cancer Research Group

The members of the UGI Cancer Research Group have published results of their large-scale prevention trials, etiologic research, and early detection research. Selected publications are listed below.

Trials

The group has conducted three chemoprevention trials. Two of them -- the Linxian General Population Nutrition Intervention Trial (NIT) and the Linxian Dysplasia NIT were conducted between 1985 and 1991 and used cancer incidence and mortality as outcome. The third -- the Chemoregression Trial -- was conducted between 1999 and 2000 and used change in dysplasia, an intermediate endpoint, as outcome. Methods and results of these trials are published in the following papers:

1. Joshi N, Johnson LL, Wei WQ, Abnet CC, Dong ZW, Taylor PR, Limburg PJ, Dawsey SM, Qiao YL, Kirsch IR. Gene expression differences in normal esophageal mucoasa associated with regression and progression of mild and moderate squamous dysplasia in a high-risk Chinese population. *Cancer Res.* 2006 Jul; 66(13):6851-60.
2. Joshi N, Johnson LL, Wei WQ, Abnet CC, Dong ZW, Taylor PR, Limburg PJ, Dawsey SM, Qiao YL, Kirsch IR. Selenomethionine treatment does not alter gene expression in normal squamous esophageal mucosa in a high-risk Chinese population. *Cancer Epidemiol Biomarkers Prev.* 2006 May;15(5):1046-7.
3. Limburg PJ, Wei W, Ahnen DJ, Qiao Y, Hawk ET, Wang G, Giffen CA, Wang G, Roth MJ, Lu N, Korn EL, Ma Y, Caldwell KL, Dong Z, Taylor PR, Dawsey SM. Randomized, placebo-controlled, esophageal squamous cell cancer chemoprevention trial of selenomethionine and celecoxib. *Gastroenterology.* 2005 Sep;129(3):863-73.
4. Dawsey SM, Wang GQ, Taylor PR, Li JY, Blot WJ, Li B, Lewin KJ, Liu FS, Weinstein WM, Wiggert S, et al. Effects of vitamin/mineral supplementation on the prevalence of histological dysplasia and early cancer of the esophagus and stomach: results from the Dysplasia Trial in Linxian, China. *Cancer Epidemiol Biomarkers Prev.* 1994 Mar;3(2):167-72.

5. Wang GQ, Dawsey SM, Li JY, Taylor PR, Li B, Blot WJ, Weinstein WM, Liu FS, Lewin KJ, Wang H, et al. Effects of vitamin/mineral supplementation on the prevalence of histological dysplasia and early cancer of the esophagus and stomach: results from the General Population Trial in Linxian, China. *Cancer Epidemiol Biomarkers Prev.* 1994 Mar;3(2):161-6.
6. Blot WJ, Li JY, Taylor PR, Guo W, Dawsey S, Wang GQ, Yang CS, Zheng SF, Gail M, Li GY, et al. Nutrition intervention trials in Linxian, China: supplementation with specific vitamin/mineral combinations, cancer incidence, and disease-specific mortality in the general population. *J Natl Cancer Inst.* 1993 Sep 15;85(18):1483-92.
7. Li B, Taylor PR, Li JY, Dawsey SM, Wang W, Tangrea JA, Liu BQ, Ershow AG, Zheng SF, Fraumeni JF Jr, et al. Linxian nutrition intervention trials. Design, methods, participant characteristics, and compliance. *Ann Epidemiol.* 1993 Nov;3(6):577-85.
8. Li JY, Taylor PR, Li B, Dawsey S, Wang GQ, Ershow AG, Guo W, Liu SF, Yang CS, Shen Q, et al. Nutrition intervention trials in Linxian, China: multiple vitamin/mineral supplementation, cancer incidence, and disease-specific mortality among adults with esophageal dysplasia. *J Natl Cancer Inst.* 1993 Sep 15;85(18):1492-8.

Etiology

This group has published extensively on environmental and genetic etiologies of UGI cancers. Etiologic research includes, but is not limited to, the role of vitamins/minerals, fruit and vegetables, smoking and alcohol consumption, polycyclic aromatic hydrocarbons, *H. pylori*, human papillomavirus, oral health, acid reflux, body mass index, and genetic factors in causing these cancers.

Vitamins/minerals

1. Abnet CC, Lai B, Qiao YL, Vogt S, Luo XM, Taylor PR, Dong ZW, Mark SD, Dawsey SM. Zinc concentration in esophageal biopsy specimens measured by x-ray fluorescence and esophageal cancer risk. *J Natl Cancer Inst.* 2005 Feb 16;97(4):301-6.
2. Taylor PR, Qiao YL, Abnet CC, Dawsey SM, Yang CS, Gunter EW, Wang W, Blot WJ, Dong ZW, Mark SD. Prospective study of serum vitamin E levels and esophageal and gastric cancers. *J Natl Cancer Inst.* 2003 Sep 17;95(18):1414-6.
3. Abnet CC, Qiao YL, Dawsey SM, Buckman DW, Yang CS, Blot WJ, Dong ZW, Taylor PR, Mark SD. Prospective study of serum retinol, beta-carotene, beta-cryptoxanthin, and lutein/zeaxanthin and esophageal and gastric cancers in China. *Cancer Causes Control.* 2003 Sep;14(7):645-55.
4. Mark SD, Qiao YL, Dawsey SM, Wu YP, Katki H, Gunter EW, Fraumeni JF Jr, Blot WJ, Dong ZW, Taylor PR. Prospective study of serum selenium levels and incident esophageal and gastric cancers. *J Natl Cancer Inst.* 2000 Nov 1;92(21):1753-63.

Fruit and vegetables

1. Tran GD, Sun XD, Abnet CC, Fan JH, Dawsey SM, Dong ZW, Mark SD, Qiao YL, Taylor PR. Prospective study of risk factors for esophageal and gastric cancers in the Linxian general population trial cohort in China. *Int J Cancer.* 2005 Jan 20;113(3):456-63.
2. Nouraie M, Pietinen P, Kamangar F, Dawsey SM, Abnet CC, Albanes D, Virtamo J, Taylor PR. Fruits, vegetables, and antioxidants and risk of gastric cancer among male smokers. *Cancer Epidemiol Biomarkers Prev.* 2005 Sep;14(9):2087-92.

Smoking and alcohol consumption

1. Freedman ND, Schatzkin A, Leitzmann MF, Hollenbeck AR, Abnet CC. Alcohol and head and neck cancer risk in a prospective study. *Br J Cancer.* 2007 Mar 27; [Epub ahead of print]

2. Chow WH, Swanson CA, Lissowska J, Groves FD, Sobin LH, Nasierowska-Guttmejer A, Radziszewski J, Regula J, Hsing AW, Jagannatha S, Zatonski W, Blot WJ. Risk of stomach cancer in relation to consumption of cigarettes, alcohol, tea and coffee in Warsaw, Poland. *Int J Cancer*. 1999 Jun 11;81(6):871-6.
3. Gammon MD, Schoenberg JB, Ahsan H, Risch HA, Vaughan TL, Chow WH, Rotterdam H, West AB, Dubrow R, Stanford JL, Mayne ST, Farrow DC, Niwa S, Blot WJ, Fraumeni JF Jr. Tobacco, alcohol, and socioeconomic status and adenocarcinomas of the esophagus and gastric cardia. *J Natl Cancer Inst*. 1997 Sep 3;89(17):1277-84.
4. Ji BT, Chow WH, Yang G, McLaughlin JK, Gao RN, Zheng W, Shu XO, Jin F, Fraumeni JF Jr, Gao YT. The influence of cigarette smoking, alcohol, and green tea consumption on the risk of carcinoma of the cardia and distal stomach in Shanghai, China. *Cancer*. 1996 Jun 15;77(12):2449-57.

Polycyclic aromatic hydrocarbons

1. Fagundes RB, Abnet CC, Strickland PT, Kamangar F, Roth MJ, Taylor PR, Dawsey SM. Higher urine 1-hydroxy pyrene glucuronide (1-OHPG) is associated with tobacco smoke exposure and drinking mate in healthy subjects from Rio Grande do Sul, Brazil. *BMC Cancer*. 2006 May 26;6:139.
2. Kamangar F, Strickland PT, Pourshams A, Malekzadeh R, Boffetta P, Roth MJ, Abnet CC, Saadatian-Elahi M, Rakhshani N, Brennan P, Etemadi A, Dawsey SM. High exposure to polycyclic aromatic hydrocarbons may contribute to high risk of esophageal cancer in northeastern Iran. *Anticancer Res*. 2005 Jan-Feb;25(1B):425-8.
3. van Gijssel HE, Divi RL, Olivero OA, Roth MJ, Wang GQ, Dawsey SM, Albert PS, Qiao YL, Taylor PR, Dong ZW, Schrager JA, Kleiner DE, Poirier MC. Semiquantitation of polycyclic aromatic hydrocarbon-DNA adducts in human esophagus by immunohistochemistry and the automated cellular imaging system. *Cancer Epidemiol Biomarkers Prev*. 2002 Dec;11(12):1622-9.
4. Roth MJ, Qiao YL, Rothman N, Tangrea JA, Dawsey SM, Cho SH, Kang D, Strickland PT. High urine 1-hydroxypyrene glucuronide concentrations in Linxian, China, an area of high risk for squamous esophageal cancer. *Biomarkers*. 2001 May; 6(5):381-6.
5. Roth MJ, Guo-Qing W, Lewin KJ, Ning L, Dawsey SM, Wesley MN, Giffen C, Yong-Qiang X, Maher MM, Taylor PR. Histopathologic changes seen in

esophagectomy specimens from the high-risk region of Linxian, China: potential clues to an etiologic exposure? *Hum Pathol.* 1998 Nov;29(11):1294-8.

6. Roth MJ, Strickland KL, Wang GQ, Rothman N, Greenberg A, Dawsey SM. High levels of carcinogenic polycyclic aromatic hydrocarbons present within food from Linxian, China may contribute to that region's high incidence of oesophageal cancer. *Eur J Cancer.* 1998 Apr;34(5):757-8. No abstract available.

H. pylori

1. Kamangar F, Qiao YL, Blaser MJ, Sun XD, Katki H, Fan JH, Perez-Perez GI, Abnet CC, Zhao P, Mark SD, Taylor PR, Dawsey SM. Helicobacter pylori and oesophageal and gastric cancers in a prospective study in China. *Br J Cancer.* 2007 Jan 15;96(1):172-6. *Epub.* 2006 Dec 19.
2. Kamangar F, Dawsey SM, Blaser MJ, Perez-Perez GI, Pietinen P, Newschaffer CJ, Abnet CC, Albanes D, Virtamo J, Taylor PR. Opposing risks of gastric cardia and noncardia gastric adenocarcinomas associated with Helicobacter pylori seropositivity. *J Natl Cancer Inst.* 2006 Oct 18;98(20):1445-52.
3. Limburg P, Qiao Y, Mark S, Wang G, Perez-Perez G, Blaser M, Wu Y, Zou X, Dong Z, Taylor P, Dawsey S. Helicobacter pylori seropositivity and subsite-specific gastric cancer risks in Linxian, China. *J Natl Cancer Inst.* 2001 Feb 7;93(3):226-33.
4. Chow WH, Blaser MJ, Blot WJ, Gammon MD, Vaughan TL, Risch HA, Perez-Perez GI, Schoenberg JB, Stanford JL, Rotterdam H, West AB, Fraumeni JF Jr. An inverse relation between cagA+ strains of Helicobacter pylori infection and risk of esophageal and gastric cardia adenocarcinoma. *Cancer Res.* 1998 Feb 15;58(4):588-90.

Human papillomavirus

1. Gao GF, Roth MJ, Wei WQ, Abnet CC, Chen F, Lu N, Zhao FH, Li XQ, Wang GQ, Taylor PR, Pan QJ, Chen W, Dawsey SM, Qiao YL. No association between HPV infection and the neoplastic progression of esophageal squamous cell carcinoma: result from a cross-sectional study in a high-risk region of China. *Int J Cancer.* 2006 Sep 15;119(6):1354-9.
2. Kamangar F, Qiao YL, Schiller JT, Dawsey SM, Fears T, Sun XD, Abnet CC, Zhao P, Taylor PR, Mark SD. Human papillomavirus serology and the risk of esophageal and gastric cancers: results from a cohort in a high-risk region in China. *Int J Cancer.* 2006 Aug 1;119(3):579-84.

Oral health

1. Abnet CC, Kamangar F, Dawsey SM, Stolzenberg-Solomon RZ, Albanes D, Pietinen P, Virtamo J, Taylor PR. Tooth loss is associated with increased risk of gastric non-cardia adenocarcinoma in a cohort of Finnish smokers. *Scand J Gastroenterol*. 2005 Jun;40(6):681-7.
2. Wei WQ, Abnet CC, Lu N, Roth MJ, Wang GQ, Dye BA, Dong ZW, Taylor PR, Albert P, Qiao YL, Dawsey SM. Risk factors for oesophageal squamous dysplasia in adult inhabitants of a high risk region of China. *Gut*. 2005 Jun;54(6):759-63.
3. Sepehr A, Kamangar F, Fahimi S, Saidi F, Abnet CC, Dawsey SM. Poor oral health as a risk factor for esophageal squamous dysplasia in northeastern Iran. *Anticancer Res*. 2005 Jan-Feb;25(1B):543-6.
4. Abnet CC, Qiao YL, Dawsey SM, Dong ZW, Taylor PR, Mark SD. Tooth loss is associated with increased risk of total death and death from upper gastrointestinal cancer, heart disease, and stroke in a Chinese population-based cohort. *Int J Epidemiol*. 2005 Apr;34(2):467-74. Epub 2005 Jan 19.
5. Abnet CC, Qiao YL, Mark SD, Dong ZW, Taylor PR, Dawsey SM. Prospective study of tooth loss and incident esophageal and gastric cancers in China. *Cancer Causes Control*. 2001 Nov;12(9):847-54.

Acid reflux

1. Ye W, Chow WH, Lagergren J, Yin L, Nyren O. Risk of adenocarcinomas of the esophagus and gastric cardia in patients with gastroesophageal reflux diseases and after antireflux surgery. *Gastroenterology*. 2001 Dec;121(6):1286-93.
2. Chow WH, Finkle WD, McLaughlin JK, Frankl H, Ziel HK, Fraumeni JF Jr. The relation of gastroesophageal reflux disease and its treatment to adenocarcinomas of the esophagus and gastric cardia. *JAMA*. 1995 Aug 9;274(6):474-7.

Body mass index

1. Chow WH, Blot WJ, Vaughan TL, Risch HA, Gammon MD, Stanford JL, Dubrow R, Schoenberg JB, Mayne ST, Farrow DC, Ahsan H, West AB, Rotterdam H, Niwa S, Fraumeni JF Jr. Body mass index and risk of adenocarcinomas of the esophagus and gastric cardia. *J Natl Cancer Inst*. 1998 Jan 21;90(2):150-5.
2. Ji BT, Chow WH, Yang G, McLaughlin JK, Gao RN, Zheng W, Shu XO, Jin F, Fraumeni JF Jr, Gao YT. Body mass index and the risk of cancers of the gastric cardia and distal stomach in Shanghai, China. *Cancer Epidemiol Biomarkers Prev*. 1997 Jul;6(7):481-5.

Genetic factors

1. Hold GL, Rabkin CS, Chow WH, Smith MG, Gammon MD, Risch HA, Vaughan TL, McColl KE, Lissowska J, Zatonski W, Schoenberg JB, Blot WJ, Mowat NA, Fraumeni JF Jr, El-Omar EM. A functional polymorphism of toll-like receptor 4 gene increases risk of gastric carcinoma and its precursors. *Gastroenterology*. 2007 Mar;132(3):905-12.
2. Hou L, El-Omar EM, Chen J, Grillo P, Rabkin CS, Baccarelli A, Yeager M, Chanock SJ, Zatonski W, Sobin LH, Lissowska J, Fraumeni JF Jr, Chow WH. Polymorphisms in Th1-type cell-mediated response genes and risk of gastric cancer. *Carcinogenesis*. 2007 Jan;28(1):118-23.
3. Kamangar F, Cheng C, Abnet CC, Rabkin CS. Interleukin-1B polymorphisms and gastric cancer risk--a meta-analysis. *Cancer Epidemiol Biomarkers Prev*. 2006 Oct;15(10):1920-8.
4. Hu N, Wang C, Hu Y, Yang HH, Kong LH, Lu N, Su H, Wang QH, Goldstein AM, Buetow KH, Emmert-Buck MR, Taylor PR, Lee MP. Genome-wide loss of heterozygosity and copy number alteration in esophageal squamous cell carcinoma using the Affymetrix GeneChip Mapping 10 K array. *BMC Genomics*. 2006 Nov 29;7:299.
5. Kamangar F, Abnet CC, Hutchinson AA, Newschaffer CJ, Helzlsouer K, Shugart YY, Pietinen P, Dawsey SM, Albanes D, Virtamo J, Taylor PR. Polymorphisms in inflammation-related genes and risk of gastric cancer (Finland). *Cancer Causes Control*. 2006 Feb;17(1):117-25.
6. Hu N, Wang C, Hu Y, Yang HH, Giffen C, Tang ZZ, Han XY, Goldstein AM, Emmert-Buck MR, Buetow KH, Taylor PR, Lee MP. Genome-wide association study in esophageal cancer using GeneChip mapping 10K array. *Cancer Res*. 2005 Apr 1;65(7):2542-6.
7. Gammon MD, Terry MB, Arber N, Chow WH, Risch HA, Vaughan TL, Schoenberg JB, Mayne ST, Stanford JL, Dubrow R, Rotterdam H, West AB, Fraumeni JF Jr, Weinstein IB, Hibshoosh H. Nonsteroidal anti-inflammatory drug use associated with reduced incidence of adenocarcinomas of the esophagus and gastric cardia that overexpress cyclin D1: a population-based study. *Cancer Epidemiol Biomarkers Prev*. Jan 2004; 13(1):34-9.
8. Roth MJ, Abnet CC, Johnson LL, Mark SD, Dong ZW, Taylor PR, Dawsey SM, Qiao YL. Polymorphic variation of Cyp1A1 is associated with the risk of gastric cardia cancer: a prospective case-cohort study of cytochrome P-450 1A1 and GST enzymes. *Cancer Causes Control*. 2004 Dec;15(10):1077-83.

9. Ratnasinghe LD, Abnet C, Qiao YL, Modali R, Stolzenberg-Solomon R, Dong ZW, Dawsey SM, Mark SD, Taylor PR. Polymorphisms of XRCC1 and risk of esophageal and gastric cardia cancer. *Cancer Lett.* 2004 Dec 28;216(2):157-64.
10. Savage SA, Abnet CC, Haque K, Mark SD, Qiao YL, Dong ZW, Dawsey SM, Taylor PR, Chanock SJ. Polymorphisms in interleukin -2, -6, and -10 are not associated with gastric cardia or esophageal cancer in a high-risk Chinese population. *Cancer Epidemiol Biomarkers Prev.* 2004 Sep;13(9):1547-9.
11. El-Omar EM, Rabkin CS, Gammon MD, Vaughan TL, Risch HA, Schoenberg JB, Stanford JL, Mayne ST, Goedert J, Blot WJ, Fraumeni JF Jr, Chow WH. Increased risk of noncardia gastric cancer associated with proinflammatory cytokine gene polymorphisms. *Gastroenterology.* 2003 May;124(5):1193-201.
12. El-Omar EM, Carrington M, Chow WH, McColl KE, Bream JH, Young HA, Herrera J, Lissowska J, Yuan CC, Rothman N, Lanyon G, Martin M, Fraumeni JF Jr, Rabkin CS. Interleukin-1 polymorphisms associated with increased risk of gastric cancer. *Nature.* 2000 Mar 23;404(6776):398-402.

Other risk factors

1. Mayne ST, Risch HA, Dubrow R, Chow WH, Gammon MD, Vaughan TL, Borchardt L, Schoenberg JB, Stanford JL, West AB, Rotterdam H, Blot WJ, Fraumeni JF Jr. Carbonated soft drink consumption and risk of esophageal adenocarcinoma. *J Natl Cancer Inst.* 2006 Jan 4;98(1):72-5.
2. Engel LS, Chow WH, Vaughan TL, Gammon MD, Risch HA, Stanford JL, Schoenberg JB, Mayne ST, Dubrow R, Rotterdam H, West AB, Blaser M, Blot WJ, Gail MH, Fraumeni JF Jr. Population attributable risks of esophageal and gastric cancers. *J Natl Cancer Inst.* 2003 Sep 17;95(18):1404-13.
3. Engel LS, Vaughan TL, Gammon MD, Chow WH, Risch HA, Dubrow R, Mayne ST, Rotterdam H, Schoenberg JB, Stanford JL, West AB, Blot WJ, Fraumeni JF Jr. Occupation and risk of esophageal and gastric cardia adenocarcinoma. *Am J Ind Med.* 2002 Jul;42(1):11-22.
4. Farrow DC, Vaughan TL, Hansten PD, Stanford JL, Risch HA, Gammon MD, Chow WH, Dubrow R, Ahsan H, Mayne ST, Schoenberg JB, West AB, Rotterdam H, Fraumeni JF Jr, Blot WJ. Use of aspirin and other nonsteroidal anti-inflammatory drugs and risk of esophageal and gastric cancer. *Cancer Epidemiol Biomarkers Prev.* 1998 Feb;7(2):97-102.
5. Hansson LE, Nyren O, Hsing AW, Bergstrom R, Josefsson S, Chow WH, Fraumeni JF Jr, Adami HO. The risk of stomach cancer in patients with

gastric or duodenal ulcer disease. *N Engl J Med.* 1996 Jul 25;335(4):242-9.

Early Detection

Esophageal cancer has a very poor prognosis, largely because symptoms occur late in the course of the disease. To reduce mortality, the group has conducted several studies on early detection of esophageal cancer using a variety of techniques.

1. Wei WQ, Abnet CC, Lu N, Roth MJ, Wang GQ, Dye BA, Dong ZW, Taylor PR, Albert P, Qiao YL, Dawsey SM. Risk factors for oesophageal squamous dysplasia in adult inhabitants of a high risk region of China. *Gut*. 2005 Jun;54(6):759-63.
2. Wang GQ, Abnet CC, Shen Q, Lewin KJ, Sun XD, Roth MJ, Qiao YL, Mark SD, Dong ZW, Taylor PR, Dawsey SM. Histological precursors of oesophageal squamous cell carcinoma: results from a 13 year prospective follow up study in a high risk population. *Gut*. 2005 Feb;54(2):187-92.
3. Dawsey SM, Fleischer DE, Wang GQ, Zhou B, Kidwell JA, Lu N, Lewin KJ, Roth MJ, Tio TL, Taylor PR. Mucosal iodine staining improves endoscopic visualization of squamous dysplasia and squamous cell carcinoma of the esophagus in Linxian, China. *Cancer*. 1998 Jul 15;83(2):220-31.
4. Roth MJ, Liu SF, Dawsey SM, Zhou B, Copeland C, Wang GQ, Solomon D, Baker SG, Giffen CA, Taylor PR. Cytologic detection of esophageal squamous cell carcinoma and precursor lesions using balloon and sponge samplers in asymptomatic adults in Linxian, China. *Cancer*. 1997 Dec 1;80(11):2047-59.
5. Dawsey SM, Shen Q, Nieberg RK, Liu SF, English SA, Cao J, Zhou B, Wang GQ, Lewin KJ, Liu FS, Roth MJ, Taylor PR. Studies of esophageal balloon cytology in Linxian, China. *Cancer Epidemiol Biomarkers Prev*. 1997 Feb;6(2):121-30.
6. Dawsey SM, Lewin KJ, Wang GQ, Liu FS, Nieberg RK, Yu Y, Li JY, Blot WJ, Li B, Taylor PR. Squamous esophageal histology and subsequent risk of squamous cell carcinoma of the esophagus. A prospective follow-up study from Linxian, China. *Cancer*. 1994 Sep 15;74(6):1686-92.