

1. Vogelstein B, Papadopoulos N, Velculescu VE, et al. Cancer genome landscapes. *Science* 2013;339:1546–1558.
2. Fearon ER, Vogelstein B. A genetic model for colorectal tumorigenesis. *Cell* 1990;61:759–767.
3. Sidransky D. Emerging molecular markers of cancer. *Nat Rev Cancer* 2002; 2:210–219.
4. Lippman SM, Levin B, Brenner DE, et al. Cancer prevention and the American Society of Clinical Oncology. *J Clin Oncol* 2004;22:3848–3851.
5. Wattenberg L. Chemoprevention of cancer. *Cancer Res* 1985;45:1–8.
6. Greenwald P, Kelloff G. The role of chemoprevention in cancer control. *IARC Scientific Publications (Lyon)* 1996;139:13–22.
7. Hanahan D, Weinberg RA. The hallmarks of cancer. *Cell* 2000;100:57–70.
8. Steele VE, Boone CW, Lubet RA, et al. Preclinical drug development paradigms for chemopreventives. *Hematol Oncol Clin North Am* 1998;12: 943–961.
9. Perloff M, Steele VE. Early-phase development of cancer prevention agents: challenges and opportunities. *Cancer Prev Res (Phila)* 2013;6:379–385.
10. National Cancer Institute. PREVENT Cancer Preclinical Drug Development Program. National Cancer Institute Web site. <http://prevention.cancer.gov/programs-resources/programs/prevent>. Accessed December 7, 2013.
11. Mehta RG, Naithani R, Huma L, et al. Efficacy of chemopreventive agents in mouse mammary gland organ culture (MMOC) model: a comprehensive review. *Curr Med Chem*. 2008;15:2785–2825.
12. Hoenerhoff MJ, Hong HH, Ton TV, et al. A review of the molecular mechanisms of chemically induced neoplasia in rat and mouse models in National Toxicology Program bioassays and their relevance to human cancer. *Toxicol Pathol* 2009;37:835–848.
13. Steele VE, Lubet RA. The use of animal models for cancer chemoprevention drug development. *Semin Oncol* 2010;37:327–338.
14. Shureiqi I, Reddy P, Brenner DE. Chemoprevention: general perspective. *Crit Rev Oncol Hematol* 2000;33:157–167.
15. Becker M. Adherence to prescribed therapies. *Med Care* 1985;23:539–554.
16. Miki Y, Swensen J, Shattuck-Eidens D, et al. A strong candidate for the breast and ovarian cancer susceptibility gene BRCA1. *Science* 1994;266:66–71.
17. Powell SM, Petersen GM, Krush AJ, et al. Molecular diagnosis of familial adenomatous polyposis. *N Engl J Med* 1993;329:1982–1987.
18. Meads C, Ahmed I, Riley RD. A systematic review of breast cancer incidence risk prediction models with meta-analysis of their performance. *Breast Cancer Res Treat* 2012;132:365–377.
19. Kastrinos F, Steyerberg EW, Balmana J, et al. Comparison of the clinical prediction model PREMM(1,2,6) and molecular testing for the systematic identification of Lynch syndrome in colorectal cancer. *Cut* 2013;62:272–279.
20. Ankerst DP, Boeck A, Freedland SJ, et al. Evaluating the PCPT risk calculator in ten international biopsy cohorts: results from the Prostate Biopsy Collaborative Group. *World J Urol* 2012;30:181–187.
21. National Institutes of Health, U.S. Food and Drug Administration. *Biomarkers and Surrogate Endpoints: Advancing Clinical Research and Applications*. Bethesda, MD: National Institutes of Health; 1999.
22. Schatzkin A, Freedman LS, Schiffman MH, et al. Validation of intermediate end points in cancer research. *J Natl Cancer Inst* 1990;82:1746–1752.
23. Prentice R. Surrogate endpoints in clinical trials: definition and operational criteria. *Statistics Med* 1989;8:431–440.
24. Ransohoff DF. Rules of evidence for cancer molecular-marker discovery and validation. *Nat Rev Cancer* 2004;4:309–314.
25. Pepe MS, Feng Z, James H, et al. Pivotal evaluation of the accuracy of a biomarker used for classification or prediction: standards for study design. *J Natl Cancer Inst* 2008;100:1432–1438.
26. Pryor WA, Stahl W, Rock CL. Beta carotene: from biochemistry to clinical trials. *Nutr Rev* 2000;58:39–53.
27. Brenner DE, Hawk E. Trials and tribulations of interrogating biomarkers to define efficacy of cancer risk reductive interventions. *Cancer Prev Res (Phila)* 2013;6:71–73.
28. Fisher B, Costantino J, Wickerham D, et al. Tamoxifen for prevention of breast cancer: report of the National Surgical Adjuvant Breast and Bowel Project P-1 study. *J Natl Cancer Inst* 1998;90:1371–1388.
29. Vogel VG, Costantino JP, Wickerham DL, et al. Update of the National Surgical Adjuvant Breast and Bowel Project Study of Tamoxifen and Raloxifene (STAR) P-2 Trial: Preventing breast cancer. *Cancer Prev Res (Phila)* 2010;3:696–706.
30. Thompson IM, Goodman PJ, Tangen CM, et al. The influence of finasteride on the development of prostate cancer. *N Engl J Med* 2003;349:215–224.
31. Omenn G, Goodman G, Thornquist M, et al. Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease. *N Engl J Med* 1996;334:1150–1155.
32. Lotan R. Retinoids in cancer chemoprevention. *Faseb J* 1996;10:1031–1039.
33. Tang X-H, Cudas LJ. Retinoids, retinoic acid receptors, and cancer. *Annu Rev Pathol* 2011;6:345–364.
34. Khachik F, Beecher G, Smith JC Jr. Lutein, lycopene, and their oxidative metabolites in chemoprevention of cancer. *J Cell Biochem* 1995;22:236–246.
35. Di Mascio P, Kaiser S, Sies H. Lycopene as the most efficient biological carotenoid singlet oxygen quencher. *Arch Biochem Biophys* 1989;274: 532–538.
36. Eroglu A, Hruszkewycz DP, dela Sena C, et al. Naturally occurring eccentric cleavage products of provitamin A beta-carotene function as antagonists of retinoic acid receptors. *J Biol Chem* 2012;287:15886–15895.
37. Ford NA, Erdman JW Jr. Are lycopene metabolites metabolically active? *Acta Biochim Pol* 2012;59:1–4.
38. World Cancer Research Fund, American Institute for Cancer Research. *Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective*. Washington, DC: AICR; 2007.
39. Panel on Dietary Antioxidants and Related Compounds, Subcommittees on Upper Reference Levels of Nutrients and Interpretation and Uses of DRIs, Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine. *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*. Washington, DC: National Academy Press; 2000.
40. Moon RC, Mehta RG, Rao KVN. Retinoids and cancer in experimental animals. In: Sporn MB, Roberts AB, Goodman DS, eds., *The Retinoids*. 2nd ed. New York: Raven Press; 1994: 573–595.
41. International Agency for Research on Cancer World Health Organization. *Carotenoids*. Lyon: International Agency for Research on Cancer; 1998.
42. Holzapfel NP, Holzapfel BM, Champ S, et al. The potential role of lycopene for the prevention and therapy of prostate cancer: from molecular mechanisms to clinical evidence. *Int J Mol Sci* 2013;14:14620–14646.
43. Hong WK, Lippman SM, Itri LM, et al. Prevention of second primary tumors with 13cRA in squamous-cell carcinoma of the head and neck. *N Engl J Med* 1990;323:795–801.
44. Benner SE, Pajak TF, Lippman SM, et al. Prevention of second primary tumors with isotretinoin in patients with squamous cell carcinoma of the head and neck: long term follow-up. *J Natl Cancer Inst* 1994;86:140–141.
45. Khuri FR, Lee JJ, Lippman SM, et al. Randomized phase III trial of low-dose isotretinoin for prevention of second primary tumors in stage I and II head and neck cancer patients. *J Natl Cancer Inst* 2006;98:441–450.
46. Bolla M, Lefur R, Ton Van J, et al. Prevention of second primary tumours with etretinate in squamous cell carcinoma of the oral cavity and oropharynx. Results of a multicentric double-blind randomised study. *Eur J Cancer* 1994; 30A:767–772.
47. Toma S, Bonelli L, Sartoris A, et al. beta-carotene supplementation in patients radically treated for stage I-II head and neck cancer: results of a randomized trial. *Oncol Rep* 2003;10:1895–1901.
48. Mayne ST, Cartmel B, Baum M, et al. Randomized trial of supplemental beta-carotene to prevent second head and neck cancer. *Cancer Res* 2001; 61:1457–1463.
49. Bairati I, Meyer F, Jobin E, et al. Antioxidant vitamins supplementation and mortality: a randomized trial in head and neck cancer patients. *Int J Cancer* 2006;119:2221–2224.
50. McLarty JW, Holiday DB, Girard WM, et al. Beta-carotene, vitamin A and lung cancer chemoprevention: results of an intermediate endpoint study. *Am J Clin Nutr* 1995;62:1431S–1438S.
51. Lee JS, Lippman SM, Benner SE, et al. Randomized placebo-controlled trial of isotretinoin in chemoprevention of bronchial squamous metaplasia. *J Clin Oncol* 1994;12:937–945.
52. The Alpha-Tocopherol Beta Carotene Cancer Prevention Study Group. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. *N Engl J Med* 1994;330:1029–1035.
53. Omenn GS, Goodman G, Thornquist M, et al. Chemoprevention of lung cancer: the beta-Carotene and Retinol Efficacy Trial (CARET) in high-risk smokers and asbestos-exposed workers. *IARC Sci Publ* 1996;67–85.
54. Hennekens CH, Buring JE, Manson JE, et al. Lack of effect of long-term supplementation with beta carotene on the incidence of malignant neoplasms and cardiovascular disease. *N Engl J Med* 1996;334:1145–1149.
55. Lee IM, Cook NR, Manson JE, et al. Beta-carotene supplementation and incidence of cancer and cardiovascular disease: the Women's Health Study. *J Natl Cancer Inst* 1999;91:2102–2106.
56. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of antioxidant vitamin supplementation in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002;360:23–33.
57. van Zandwijk N, Dalesio O, Pastorino U, et al. EUROSCAN, a randomized trial of vitamin A and N-acetylcysteine in patients with head and neck cancer or lung cancer. For the European Organization for Research and Treatment of Cancer Head and Neck and Lung Cancer Cooperative Groups. *J Natl Cancer Inst* 2000;92:977–986.
58. Lippman SM, Lee JJ, Karp DD, et al. Randomized phase III intergroup trial of isotretinoin to prevent second primary tumors in stage I non-small-cell lung cancer. *J Natl Cancer Inst* 2001;93:605–618.
59. Mayne ST, Lippman SM. Cigarettes: a smoking gun in cancer chemoprevention. *J Natl Cancer Inst* 2005;97:1319–1321.
60. Veronesi U, De Palo G, Marubini E, et al. Randomized trial of fenretinide to prevent second breast malignancy in women with early breast cancer. *J Natl Cancer Inst* 1999;91:1847–1856.
61. De Palo G, Mariani L, Camerini T, et al. Effect of fenretinide on ovarian carcinoma occurrence. *Gynecol Oncol* 2002;86:24–27.
62. Uray IP, Brown PH. Chemoprevention of hormone receptor-negative breast cancer: new approaches needed. *Recent Results Cancer Res* 2011;188:147–162.

63. Kraemer KH, DiGiovanna JJ, Moshell AN, et al. Prevention of skin cancer in xeroderma pigmentosum with the use of oral isotretinoin. *N Engl J Med* 1988;318:1633–1637.
64. Bouwes Bavinck JN, Tieben LM, Van Der Woude FJ, et al. Prevention of skin cancer and reduction of keratotic skin lesions during acitretin therapy in renal transplant recipients: a double-blind, placebo-controlled study. *J Clin Oncol* 1995;13:1933–1938.
65. Tangrea JA, Edwards BK, Taylor PR, et al. Long-term therapy with low-dose isotretinoin for prevention of basal cell carcinoma: a multicenter clinical trial. Isotretinoin-Basal Cell Carcinoma Study Group. *J Natl Cancer Inst* 1992;84:328–332.
66. Levine N, Moon TE, Cartmel B, et al. Trial of retinol and isotretinoin in skin cancer prevention: a randomized, double-blind, controlled trial. Southwest Skin Cancer Prevention Study Group. *Cancer Epidemiol Biomarkers Prev* 1997;6:957–961.
67. Moon TE, Levine N, Cartmel B, et al. Effect of retinol in preventing squamous cell skin cancer in moderate-risk subjects: a randomized, double-blind, controlled trial. Southwest Skin Cancer Prevention Study Group. *Cancer Epidemiol Biomarkers Prev* 1997;6:949–956.
68. Greenberg ER, Baron JA, Stukel TA, et al. A clinical trial of beta carotene to prevent basal-cell and squamous-cell cancers of the skin. The Skin Cancer Prevention Study Group. *N Engl J Med* 1990;323:789–895.
69. Green A, Williams G, Neale R, et al. Daily sunscreen application and beta-carotene supplementation in prevention of basal-cell and squamous-cell carcinomas of the skin: a randomised controlled trial. *Lancet* 1999;354:723–729.
70. Clark LC, Combs GF Jr, Turnbull BW, et al. Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin. A randomized controlled trial. Nutritional Prevention of Cancer Study Group. *JAMA* 1996;276:1957–1963.
71. Duffield-Lillico AJ, Slate EH, Reid ME, et al. Nutritional Prevention of Cancer Study Group. Selenium supplementation and secondary prevention of nonmelanoma skin cancer in a randomized trial. *J Natl Cancer Inst* 2003;95:1477–1481.
72. Sabichi AL, Lerner SP, Atkinson EN, et al. Phase III prevention trial of fenretinide in patients with resected non-muscle-invasive bladder cancer. *Clin Cancer Res* 2008;14:224–229.
73. Lamm DL, Riggs DR, Shriver JS, et al. Megadose vitamins in bladder cancer: a double-blind clinical trial. *J Urol* 1994;151:21–26.
74. Meyskens FL Jr, Surwit E, Moon TE, et al. Enhancement of regression of cervical intraepithelial neoplasia II (moderate dysplasia) with topically applied all-trans-retinoic acid: a randomized trial. *J Natl Cancer Inst* 1994;86:539–543.
75. Blot WJ, Li JY, Taylor PR, 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;85:1483–1492.
76. Qiao YL, Dawsey SM, Kamangar F, et al. Total and cancer mortality after supplementation with vitamins and minerals: follow-up of the Linxian General Population Nutrition Intervention Trial. *J Natl Cancer Inst* 2009;101:507–518.
77. Mayne ST, Ferrucci LM, Cartmel B. Lessons learned from randomized clinical trials of micronutrient supplementation for cancer prevention. *Annu Rev Nutr* 2012;32:369–390.
78. Li JY, Taylor PR, Li B, 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;85:1492–1498.
79. Kikendall JW, Mobarhan S, Nelson R, et al. Oral beta carotene does not reduce the recurrence of colorectal adenomas [Abstract]. *Am J Gastroenterol* 1991;36:1356.
80. MacLennan R, Macrae F, Bain C, et al. Randomized trial of intake of fat, fiber, and beta carotene to prevent colorectal adenomas. *J Natl Cancer Inst* 1995;87:1760–1766.
81. Greenberg ER, Baron JA, Tosteson TD, et al. A clinical trial of antioxidant vitamins to prevent colorectal adenoma. Polyp Prevention Study Group. *N Engl J Med* 1994;331:141–147.
82. Baron JA, Cole BF, Mott L, et al. Neoplastic and antineoplastic effects of beta-carotene on colorectal adenoma recurrence: results of a randomized trial. *J Natl Cancer Inst* 2003;95:717–722.
83. Heinonen OP, Albanes D, Virtamo J, et al. Prostate cancer and supplementation with alpha-tocopherol and beta-carotene: incidence and mortality in a controlled trial. *J Natl Cancer Inst* 1998;90:440–446.
84. Lippman SM, Klein EA, Goodman PJ, et al. Effect of selenium and vitamin E on risk of prostate cancer and other cancers: the Selenium and Vitamin E Cancer Prevention Trial (SELECT). *JAMA* 2009;301:39–51.
85. Klein EA, Thompson IM Jr, Tangen CM, et al. Vitamin E and the risk of prostate cancer: the Selenium and Vitamin E Cancer Prevention Trial (SELECT). *JAMA* 2011;306:1549–1556.
86. Gaziano JM, Glynn RJ, Christen WG, et al. Vitamins E and C in the prevention of prostate and total cancer in men: the Physicians' Health Study II randomized controlled trial. *JAMA* 2009;301:52–62.
87. Boileau TW, Liao Z, Kim S, et al. Prostate carcinogenesis in N-methyl-N-nitrosourea (NMU)-testosterone-treated rats fed tomato powder, lycopene, or energy-restricted diets. *J Natl Cancer Inst* 2003;95:1578–1586.
88. Goralczyk R. Beta-carotene and lung cancer in smokers: review of hypotheses and status of research. *Nutr Cancer* 2009;61:767–774.
89. Kristal AR, Darke AK, Morris JS, et al. Baseline Selenium Status and Effects of Selenium and Vitamin E Supplementation on Prostate Cancer Risk. *J Natl Cancer Inst* 2014;106:djt456.
90. Stone JR, Yang S. Hydrogen peroxide: a signaling messenger. *Antioxid Redox Signal* 2006;8:243–270.
91. Finkel T. Signal transduction by reactive oxygen species. *J Cell Biol* 2011;194:7–15.
92. Sayin V, Ibrahim M, Larsson E, et al. Antioxidants accelerate lung cancer progression in mice. *Sci Transl Med* 2014;6:ra15.
93. Mayne ST. Oxidative stress, dietary antioxidant supplements, and health: is the glass half full or half empty? *Cancer Epidemiol Biomarkers Prev* 2013;22:2145–2147.
94. Duthie SJ, Narayanan S, Blum S, et al. Folate deficiency in vitro induces uracil misincorporation and DNA hypomethylation and inhibits DNA excision repair in immortalized normal human colon epithelial cells. *Nutr Cancer* 2000;37:245–251.
95. Blount BC, Mack MM, Wehr CM, et al. Folate deficiency causes uracil misincorporation into human DNA and chromosome breakage: implications for cancer and neuronal damage. *Proc Natl Acad Sci U S A* 1997;94:3290–3295.
96. Giovannucci E. Epidemiologic studies of folate and colorectal neoplasia: a review. *J Nutr* 2002;132:2350S–2355S.
97. White E, Shannon JS, Patterson RE. Relationship between vitamin and calcium supplement use and colon cancer. *Cancer Epidemiol Biomarkers Prev* 1997;6:769–774.
98. Jacobs EJ, Connell CJ, Patel AV, et al. Multivitamin use and colon cancer mortality in the Cancer Prevention Study II cohort (United States). *Cancer Causes Control* 2001;12:927–934.
99. Gibson TM, Weinstein SJ, Pfeiffer RM, et al. Pre- and postfortification intake of folate and risk of colorectal cancer in a large prospective cohort study in the United States. *Am J Clin Nutr* 2011;94:1053–1062.
100. Chen J, Giovannucci E, Kelsey K, et al. A methylenetetrahydrofolate reductase polymorphism and the risk of colorectal cancer. *Cancer Res* 1996;56:4862–4864.
101. Larsson S, Giovannucci E, Wolk A. Vitamin B6 intake, alcohol consumption, and colorectal cancer: a longitudinal population-based cohort of women. *Gastroenterology* 2005;128:1830–1837.
102. Wei E, Giovannucci E, Selhub J, et al. Plasma vitamin B6 and the risk of colorectal cancer and adenoma in women. *J Natl Cancer Inst* 2005;97:684–692.
103. Giovannucci E, Rimm EB, Ascherio A, et al. Alcohol, low-methionine-low-folate diets, and risk of colon cancer in men. *J Natl Cancer Inst* 1995;87:265–273.
104. Jaszewski R, Misra S, Tobi M, et al. Folic acid supplementation inhibits recurrence of colorectal adenomas: a randomized chemoprevention trial. *World J Gastroenterol* 2008;14:4492–4498.
105. Paspatis GA, Karamanolis DG. Folate supplementation and adenomatous colonic polyps. *Dis Colon Rectum* 1994;37:1340–1341.
106. Cole BF, Baron JA, Sandler RS, et al. Folic acid for the prevention of colorectal adenomas: a randomized clinical trial. *JAMA* 2007;297:2351–2359.
107. Logan RF, Grainge MJ, Shepherd VC, et al. Aspirin and folic acid for the prevention of recurrent colorectal adenomas. *Gastroenterology* 2008;134:29–38.
108. Wu K, Platz EA, Willett WC, et al. A randomized trial on folic acid supplementation and risk of recurrent colorectal adenoma. *Am J Clin Nutr* 2009;90:1623–1631.
109. Gao Q-Y, Chen H-M, Chen Y-X, et al. Folic acid prevents the initial occurrence of sporadic colorectal adenoma in Chinese older than 50 years of age: a randomized clinical trial. *Cancer prevention research (Phila)* 2013;6:744–752.
110. Ramnath N, Kim S, Christensen PJ. Vitamin D and lung cancer. *Expert Rev Respir Med* 2011;5:305–309.
111. Deeb KK, Trump DL, Johnson CS. Vitamin D signalling pathways in cancer: potential for anticancer therapeutics. *Nat Rev Cancer* 2007;7:684–700.
112. McCullough M, Robertson AS, Rodriguez C, et al. Calcium, vitamin D, dairy products, and risk of colorectal cancer in the cancer prevention study II nutrition cohort (United States). *Cancer Causes Control* 2003;14:1–12.
113. Wu K, Willett WC, Fuchs CS, et al. Calcium intake and risk of colon cancer in women and men. *J Natl Cancer Inst* 2002;94:437–446.
114. Chung M, Balk EM, Brendel M, et al. *Vitamin D and Calcium: A Systematic Review of Health Outcomes*. Evidence Report No. 183 (Prepared by the Tufts Evidence-based Practice Center). Rockville, MD: Agency for Healthcare Research and Quality; 2009.
115. World Health Organization, International Agency for Research on Cancer. Vitamin D and Cancer. Working Group Reports, Volume 5. Lyon, France: IARC; 2008.
116. Stolzenberg-Solomon RZ, Jacobs EJ, Arslan AA, et al. Circulating 25-hydroxyvitamin D and risk of pancreatic cancer: Cohort Consortium Vitamin D Pooling Project of Rarer Cancers. *Am J Epidemiol* 2010;172:81–93.
117. Baron J, Beach M, Mandel JS, et al. Calcium supplements for the prevention of colorectal adenomas. The Calcium Polyp Prevention Study Group. *N Engl J Med* 1999;340:101–107.
118. Bonithon-Kopp C, Kronborg O, Giacosa A, et al. Calcium and fibre supplementation in prevention of colorectal adenoma recurrence: a randomized intervention trial. *Lancet* 2000;356:1300–1306.

119. Wactawski-Wende J, Kotchen JM, Anderson GL, et al. Calcium plus vitamin D supplementation and the risk of colorectal cancer. *N Engl J Med* 2006;354:684–696.
120. Trivedi DP, Doll R, Khaw KT. Effect of four monthly oral vitamin D3 (cholecalciferol) supplementation on fractures and mortality in men and women living in the community: randomised double blind controlled trial. *BMJ* 2003;326:469.
121. Cui Y, Rohan TE. Vitamin D, calcium, and breast cancer risk: a review. *Cancer Epidemiol Biomarkers Prev* 2006;15:1427–1437.
122. Chlebowski RT, Johnson KC, Kooperberg C, et al. Calcium plus vitamin D supplementation and the risk of breast cancer. *J Natl Cancer Inst* 2008;100:1581–1591.
123. Lappe JM, Travers-Gustafson D, Davies KM, et al. Vitamin D and calcium supplementation reduces cancer risk: results of a randomized trial. *Am J Clin Nutr* 2007;85:1586–1591.
124. Manson JE, Bassuk SS, Lee IM, et al. The Vitamin D and Omega-3 Trial (VITAL): rationale and design of a large randomized controlled trial of vitamin D and marine omega-3 fatty acid supplements for the primary prevention of cancer and cardiovascular disease. *Contemp Clin Trials* 2012;33:159–171.
125. Wu X, Spitz MR, Lee JJ, et al. Novel susceptibility loci for second primary tumors/recurrence in head and neck cancer patients: large-scale evaluation of genetic variants. *Cancer Prev Res (Phila)* 2009;2:617–624.
126. Platz EA. Is prostate cancer prevention with selenium all in the genes? *Cancer Prev Res (Phila)* 2010;3:576–578.
127. Miller JW, Ulrich CM. Folic acid and cancer—where are we today? *Lancet* 2013;381:974–976.
128. Thun MJ, Henley SJ, Patrono C. Nonsteroidal anti-inflammatory drugs as anticancer agents: mechanistic, pharmacologic, and clinical issues. *J Natl Cancer Inst* 2002;94:252–266.
129. Wang D, Mann JR, DuBois RN. The role of prostaglandins and other eicosanoids in the gastrointestinal tract. *Gastroenterology* 2005;128:1445–1461.
130. Gurpinar E, Grizzle WE, Piazza GA. COX-Independent Mechanisms of Cancer Chemoprevention by Anti-Inflammatory Drugs. *Front Oncol* 2013;3:181.
131. Rothwell PM, Wilson M, Price JF, et al. Effect of daily aspirin on risk of cancer metastasis: a study of incident cancers during randomised controlled trials. *Lancet* 2012;379:1591–1601.
132. Rothwell PM, Price JF, Fowkes FG, et al. Short-term effects of daily aspirin on cancer incidence, mortality, and non-vascular death: analysis of the time course of risks and benefits in 51 randomised controlled trials. *Lancet* 2012;379:1602–1612.
133. Thun MJ, Nambodiri MM, Heath C Jr. Aspirin use and reduced risk of fatal colon cancer. *N Engl J Med* 1991;325:1593–1596.
134. Chan AT, Giovannucci EL, Meyerhardt JA, et al. Aspirin dose and duration of use and risk of colorectal cancer in men. *Gastroenterology* 2008;134:21–28.
135. Chan AT, Giovannucci EL, Meyerhardt JA, et al. Long-term use of aspirin and nonsteroidal anti-inflammatory drugs and risk of colorectal cancer. *JAMA* 2005;294:914–923.
136. Liao LM, Vaughan TL, Corley DA, et al. Nonsteroidal anti-inflammatory drug use reduces risk of adenocarcinomas of the esophagus and esophagogastric junction in a pooled analysis. *Gastroenterology* 2012;142:442–452.
137. Pollard M, Luckert PH. Effect of indomethacin on intestinal tumor induced in rats by the acetate derivative of dimethylnitrosamine. *Science* 1981;214:558–559.
138. Jacoby RF, Marshall DJ, Newton MA, et al. Chemoprevention of spontaneous intestinal adenomas in the Apc Min mouse model by the nonsteroidal anti-inflammatory drug piroxicam. *Cancer Res* 1996;56:710–714.
139. Kawamori T, Rao C, Seibert K, et al. Chemopreventive effect of celecoxib, a specific cyclooxygenase-2 inhibitor on colon carcinogenesis. *Cancer Res* 1998;58:409–412.
140. Oshima M, Dinchuk JE, Kargman SL. Suppression of intestinal polyposis in Apc delta 716 knockout mice by inhibition of cyclooxygenase 2 (COX-2). *Cell* 1996;87:803–809.
141. Anderson WF, Umar A, Viner JL, et al. The role of cyclooxygenase inhibitors in cancer prevention. *Curr Pharm Des* 2002;8:1055–1062.
142. Giardiello FM, Yang VW, Hylind LM, et al. Primary chemoprevention of familial adenomatous polyposis with sulindac. *N Engl J Med* 2002;346:1054–1059.
143. Steinbach G, Lynch PM, Phillips RK. The effect of celecoxib, a cyclooxygenase-2 inhibitor, in familial adenomatous polyposis. *N Engl J Med* 2000;342:1946–1952.
144. Thorson AG, Lynch HT, Smyrk TC. Rectal cancer in FAP patient after sulindac. *Lancet* 1994;343:180.
145. Calaluce R, Earnest DL, Heddens D, et al. Effects of piroxicam on prostaglandin E2 levels in rectal mucosa of adenomatous polyp patients: a randomized phase IIb trial. *Cancer Epidemiol Biomarkers Prev* 2000;9:1287–1292.
146. Ladenheim J, Garcia G, Titzer D, et al. Effects of sulindac on sporadic colonic polyps. *Gastroenterology* 1995;108:1083–1087.
147. Meyskens FL Jr, McLaren CE, Pelot D, et al. Difluoromethylornithine plus sulindac for the prevention of sporadic colorectal adenomas: a randomized placebo-controlled, double-blind trial. *Cancer Prev Res (Phila)* 2008;1:32–38.
148. Arber N, Eagle CJ, Spicak J, et al. Celecoxib for the prevention of colorectal adenomatous polyps. *N Engl J Med* 2006;355:885–895.
149. Bertagnolli MM, Eagle CJ, Zauber AG, et al. Celecoxib for the prevention of sporadic colorectal adenomas. *N Engl J Med* 2006;355:873–884.
150. Baron JA, Sandler RS, Bresalier RS, et al. A randomized trial of rofecoxib for the chemoprevention of colorectal adenomas. *Gastroenterology* 2006;131:1674–1682.
151. Bresalier RS, Sandler RS, Quan H, et al. Cardiovascular events associated with rofecoxib in a colorectal adenoma chemoprevention trial. *N Engl J Med* 2005;352:1092–1102.
152. Solomon SD, McMurray JJ, Pfeffer MA, et al. Cardiovascular risk associated with celecoxib in a clinical trial for colorectal adenoma prevention. *N Engl J Med* 2005;352:1071–1080.
153. Rostom A, Dube C, Lewin G, et al. Nonsteroidal anti-inflammatory drugs and cyclooxygenase-2 inhibitors for primary prevention of colorectal cancer: a systematic review prepared for the U.S. Preventive Services Task Force. *Ann Intern Med* 2007;146:376–389.
154. Dube C, Rostom A, Lewin G, et al. The use of aspirin for primary prevention of colorectal cancer: a systematic review prepared for the U.S. Preventive Services Task Force. *Ann Intern Med* 2007;146:365–375.
155. Rothwell PM, Fowkes FG, Belch JF, et al. Effect of daily aspirin on long-term risk of death due to cancer: analysis of individual patient data from randomised trials. *Lancet* 2011;377:31–41.
156. Rothwell PM. Aspirin in prevention of sporadic colorectal cancer: current clinical evidence and overall balance of risks and benefits. *Recent Results Cancer Res* 2013;191:121–142.
157. U.S. Preventive Services Task Force. Routine aspirin or nonsteroidal anti-inflammatory drugs for the primary prevention of colorectal cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2007;146:361–364.
158. Mulshine JL, Atkinson JC, Greer RO, et al. Randomized, double-blind, placebo-controlled phase IIb trial of the cyclooxygenase inhibitor ketorolac as an oral rinse in oropharyngeal leukoplakia. *Clin Cancer Res* 2004;10:1565–1573.
159. Mao JT, Fishbein MC, Adams B, et al. Celecoxib decreases Ki-67 proliferative index in active smokers. *Clin Cancer Res* 2006;12:314–320.
160. Bord S, Horner A, Beavan S, et al. Estrogen receptors alpha and beta are differentially expressed in developing human bone. *J Clin Endocrinol Metab* 2001;86:2309–2314.
161. Kuiper GG, Carlsson B, Grandien K, et al. Comparison of the ligand binding specificity and transcript tissue distribution of estrogen receptors alpha and beta. *Endocrinology* 1997;138:863–870.
162. Fabian CJ, Kimler BF. Selective estrogen-receptor modulators for primary prevention of breast cancer. *J Clin Oncol* 2005;23:1644–1655.
163. Jordan VC. SERMs: meeting the promise of multifunctional medicines. *J Natl Cancer Inst* 2007;99:350–356.
164. Jordan VC. Tamoxifen (ICI46,474) as a targeted therapy to treat and prevent breast cancer. *Br J Pharmacol* 2006;147:S269–S276.
165. Jordan VC. Effect of tamoxifen (ICI 46,474) on initiation and growth of DMBA-induced rat mammary carcinomas. *Eur J Cancer* 1976;12:419–424.
166. Jordan VC. Chemoprevention of breast cancer with selective oestrogen-receptor modulators. *Nat Rev Cancer* 2007;7:46–53.
167. Cuzick J, Baum M. Tamoxifen and contralateral breast cancer. *Lancet* 1985;2:282.
168. Fisher B, Redmond C. New perspective on cancer of the contralateral breast: a marker for assessing tamoxifen as a preventive agent. *J Natl Cancer Inst* 1991;83:1278–1280.
169. Ettinger B, Black DM, Mitlak BH, et al. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: results from a 3-year randomized clinical trial. Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators. *JAMA* 1999;282:637–645.
170. LaCroix AZ, Powles T, Osborne CK, et al. Breast cancer incidence in the randomized PEARL trial of lasofoxifene in postmenopausal osteoporotic women. *J Natl Cancer Inst* 2010;102:1706–1715.
171. Cummings SR, Ensrud K, Delmas PD, et al. Lasofoxifene in postmenopausal women with osteoporosis. *N Engl J Med* 2010;362:686–696.
172. Cummings SR, McClung M, Reginster JY, et al. Arzoxifene for prevention of fractures and invasive breast cancer in postmenopausal women. *J Bone Miner Res* 2011;26:397–404.
173. Powles TJ, Diem SJ, Fabian CJ, et al. Breast cancer incidence in postmenopausal women with osteoporosis or low bone mass using arzoxifene. *Breast Cancer Res Treat* 2012;134:299–306.
174. Nelson HD, Smith ME, Griffin JC, et al. Use of medications to reduce risk for primary breast cancer: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med* 2013;158:604–614.
175. Moyer VA. Medications for risk reduction of primary breast cancer in women: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2013;159:698–708.
176. Viswanathan K, Hurley P, Bantug E, et al. Use of pharmacologic interventions for breast cancer risk reduction: American Society of Clinical Oncology clinical practice guideline. *J Clin Oncol* 2013;31:2942–2962.
177. Vogel VG, Costantino JP, Wickerham DL, et al. Carcinoma in situ outcomes in National Surgical Adjuvant Breast and Bowel Project Breast Cancer Chemoprevention Trials. *J Natl Cancer Inst Monogr* 2010;2010:181–186.

178. Cuzick J, Sestak I, Bonanni B, et al. Selective oestrogen receptor modulators in prevention of breast cancer: an updated meta-analysis of individual participant data. *Lancet* 2013;381:1827–1834.
179. Barrett-Connor E, Mosca L, Collins P, et al. Effects of raloxifene on cardiovascular events and breast cancer in postmenopausal women. *N Engl J Med* 2006;355:125–137.
180. Snyder KR, Sparano N, Malinowski JM. Raloxifene hydrochloride. *Am J Health Syst Pharm* 2000;57:1669–1675.
181. Goss PE, Ingle JN, Martino S, et al. A randomized trial of letrozole in postmenopausal women after five years of tamoxifen therapy for early-stage breast cancer. *N Engl J Med* 2003;349:1793–1802.
182. Fabian CJ, Kimler BF, Zalles CM, et al. Reduction in proliferation with six months of letrozole in women on hormone replacement therapy. *Breast Cancer Res Treat* 2007;106:75–84.
183. Goss PE, Ingle JN, Ales-Martinez JE, et al. Exemestane for breast-cancer prevention in postmenopausal women. *N Engl J Med* 2011;364:2381–2391.
184. Cheung AM, Tile L, Cardew S, et al. Bone density and structure in healthy postmenopausal women treated with exemestane for the primary prevention of breast cancer: a nested substudy of the MAP.3 randomised controlled trial. *Lancet Oncol* 2012;13:275–284.
185. Cuzick J, Sestak I, Forbes JF, et al. Anastrozole for prevention of breast cancer in high-risk postmenopausal women (IBIS-II): an international, double-blind, randomised placebo-controlled trial. *Lancet* 2014;383:1041–1048.
186. Waters EA, McNeel TS, Stevens WM, et al. Use of tamoxifen and raloxifene for breast cancer chemoprevention in 2010. *Breast Cancer Res Treat* 2012;134:875–880.
187. King MC, Wieand S, Hale K, et al. Tamoxifen and breast cancer incidence among women with inherited mutations in BRCA1 and BRCA2: National Surgical Adjuvant Breast and Bowel Project (NSABP-P1) Breast Cancer Prevention Trial. *JAMA* 2001;286:2251–2256.
188. Gronwald J, Tung N, Foulkes WD, et al. Tamoxifen and contralateral breast cancer in BRCA1 and BRCA2 carriers: an update. *Int J Cancer* 2006;118:2281–2284.
189. Hess-Wilson JK, Knudsen KE. Endocrine disrupting compounds and prostate cancer. *Cancer Lett* 2006;241:1–12.
190. Andriole G, Bostwick D, Civantos F, et al. The effects of 5 α -reductase inhibitors on the natural history, detection and grading of prostate cancer: current state of knowledge. *J Urol* 2005;174:2098–2104.
191. Thompson IM, Tangen CM, Goodman PJ, et al. Chemoprevention of prostate cancer. *J Urol* 2009;182:499–507.
192. Andriole GL, Bostwick DG, Brawley OW, et al. Effect of dutasteride on the risk of prostate cancer. *N Engl J Med* 2010;362:1192–1202.
193. Thompson IM Jr, Goodman PJ, Tangen CM, et al. Long-term survival of participants in the prostate cancer prevention trial. *N Engl J Med* 2013;369:603–610.
194. Gerner EW, Meyskens FL Jr. Polyamines and cancer: old molecules, new understanding. *Nat Rev Cancer* 2004;4:781–792.
195. Meyskens FL Jr, Gerner EW. Development of difluoromethylornithine (DFMO) as a chemoprevention agent. *Clin Cancer Res* 1999;5:945–951.
196. Love R, Carbone P, Verma A, et al. Randomized phase I chemoprevention dose seeking study of alpha-difluoromethylornithine. *J Natl Cancer Inst* 1993;85:732–737.
197. Alberts DS, Dorr RT, Einspahr JG, et al. Chemoprevention of human actinic keratoses by topical 2-(difluoromethyl)-dl-ornithine. *Cancer Epidemiol Biomarkers Prev* 2000;9:1281–1286.
198. Meyskens FL Jr, Surwit E, Moon TE, et al. Enhancement of regression of cervical intraepithelial neoplasia II (moderate dysplasia) with topically applied all-trans-retinoic acid: randomized trial. *J Natl Cancer Inst* 1994;86:539–543.
199. Fabian CJ, Kimler BF, Brady DA, et al. A phase II breast cancer chemoprevention trial of oral alpha-difluoromethylornithine: breast tissue, imaging, and serum and urine biomarkers. *Clin Cancer Res* 2002;8:3105–3117.
200. Jeter JM, Alberts DS. Difluoromethylornithine: the proof is in the polyamines. *Cancer Prev Res (Phila)* 2012;5:1341–1344.
201. Gronich N, Rennert G. Beyond aspirin-cancer prevention with statins, metformin and bisphosphonates. *Nat Rev Clin Oncol* 2013;10:625–642.
202. Moyad MA. Why a statin and/or another proven heart healthy agent should be utilized in the next major cancer chemoprevention trial: part II. *Urologic Oncol* 2004;22:472–477.
203. Bertagnolli MM, Hsu M, Hawk ET, et al. Statin use and colorectal adenoma risk: results from the adenoma prevention with celecoxib trial. *Cancer Prev Res (Phila)* 2010;3:588–596.
204. Simon MS, Rosenberg CA, Rodabough RJ, et al. Prospective analysis of association between use of statins or other lipid-lowering agents and colorectal cancer risk. *Ann Epidemiol* 2012;22:17–27.
205. Platz EA, Leitzmann MF, Viswanathan K, et al. Statin drugs and risk of advanced prostate cancer. *J Natl Cancer Inst* 2006;98:1819–1825.
206. Eliassen AH, Colditz GA, Rosner B, et al. Serum lipids, lipid-lowering drugs, and the risk of breast cancer. *Arch Intern Med* 2005;165:2264–2271.
207. Lipkin SM, Chao EC, Moreno V, et al. Genetic variation in 3-hydroxy-3-methylglutaryl CoA reductase modifies the chemopreventive activity of statins for colorectal cancer. *Cancer Prev Res (Phila)* 2010;3:597–603.
208. Rennert G. Bisphosphonates: beyond prevention of bone metastases. *J Natl Cancer Inst* 2011;103:1728–1729.
209. Rennert G, Pinchev M, Rennert HS. Use of bisphosphonates and risk of postmenopausal breast cancer. *J Clin Oncol* 2010;28:3577–3581.
210. Chlebowski RT, Chen Z, Cauley JA, et al. Oral bisphosphonate use and breast cancer incidence in postmenopausal women. *J Clin Oncol* 2010;28:3582–3590.
211. Monsees GM, Malone KE, Tang MT, et al. Bisphosphonate use after estrogen receptor-positive breast cancer and risk of contralateral breast cancer. *J Natl Cancer Inst* 2011;103:1752–1760.
212. Kirpichnikov D, McFarlane SI, Sowers JR. Metformin: an update. *Ann Intern Med* 2002;137:25–33.
213. Pollack MN. Insulin, insulin-like growth factors, insulin resistance, and neoplasia. *Am J Clin Nutr* 2007;86:s820–s822.
214. Evans JM, Donnelly LA, Emslie-Smith AM, et al. Metformin and reduced risk of cancer in diabetic patients. *BMJ* 2005;330:1304–1305.
215. Zhu P, Davis M, Blackwelder A, et al. Metformin selectively targets tumor initiating cells in erbB-2 overexpressing breast cancer models. *Cancer Prev Res (Phila)* 2014;7:199–210.
216. Lonardo E, Cioffi M, Sancho P, et al. Metformin targets the metabolic Achilles heel of human pancreatic cancer stem cells. *PLoS One* 2013;8:e76518.
217. Grubbs C, Clapper M, Reid J, et al. *Metformin Promotes Tumorigenesis in Animal Models of Cancer Prevention*. Washington, DC: American Association for Cancer Research; 2013.
218. Chlebowski RT, McTiernan A, Wactawski-Wende J, et al. Diabetes, metformin, and breast cancer in postmenopausal women. *J Clin Oncol* 2012;30:2844–2852.
219. Heger M, van Golen RF, Broekgaarden D, et al. The molecular basis for the pharmacokinetics and pharmacodynamics of curcumin and its metabolites in relation to cancer. *Pharmacol Rev* 2014;66:222–307.
220. Whitlock NC, Baek SJ. The anticancer effects of resveratrol: modulation of transcription factors. *Nutr Cancer* 2012;64:493–502.
221. Lambert JD. Does tea prevent cancer? Evidence from laboratory and human intervention studies. *Am J Clin Nutr* 2013;98:1667S–1675S.
222. Kakarala M, Brenner DE, Korkaya H, et al. Targeting breast stem cells with the cancer preventive compounds curcumin and piperine. *Breast Cancer Res Treat* 2010;122:777–785.
223. Norris L, Karmokar A, Howells L, et al. The role of cancer stem cells in the anti-carcinogenicity of curcumin. *Mol Nutr Food Res* 2013;57:1630–1637.
224. Zou H, Yuan C, Dong L, et al. Human cyclooxygenase-1 activity and its responses to COX inhibitors are allosterically regulated by nonsubstrate fatty acids. *J Lipid Res* 2012;53:1336–1347.
225. Wada M, Delong CJ, Hong YH, et al. Enzymes and receptors of prostaglandin pathways with arachidonic acid- vs. eicosapentaenoic acid-derived substrates and products. *J Biol Chem* 2007;282:22254–22266.
226. Laviano A, Rianda S, Molino A, et al. Omega-3 fatty acids in cancer. *Curr Opin Clin Nutr Metab Care* 2013;16:156–161.
227. Cockbain AJ, Toogood GJ, Hull MA. Omega-3 polyunsaturated fatty acids for the treatment and prevention of colorectal cancer. *Cut* 2012;61:135–149.
228. Stoner GD, Wang LS, Casto BC. Laboratory and clinical studies of cancer chemoprevention by antioxidants in berries. *Carcinogenesis* 2008;29:1665–1674.
229. Wang LS, Dombkowski AA, Seguin C, et al. Mechanistic basis for the chemopreventive effects of black raspberries at a late stage of rat esophageal carcinogenesis. *Mol Carcinog* 2011;50:291–300.
230. Wang LS, Kuo CT, Stoner K, et al. Dietary black raspberries modulate DNA methylation in dextran sodium sulfate (DSS)-induced ulcerative colitis. *Carcinogenesis* 2013;34:2842–2850.
231. Ireson C, Orr S, Jones DJ, et al. Characterization of metabolites of the chemopreventive agent curcumin in human and rat hepatocytes and in the rat in vivo, and evaluation of their ability to inhibit phorbol ester-induced prostaglandin E2 production. *Cancer Res* 2001;61:1058–1064.
232. Ireson CR, Jones DJ, Orr S, et al. Metabolism of the cancer chemopreventive agent curcumin in human and rat intestine. *Cancer Epidemiol Biomarkers Prev* 2002;11:105–111.
233. Vared SK, Kakarala M, Ruffin MT, et al. Pharmacokinetics of curcumin conjugate metabolites in healthy human subjects. *Cancer Epidemiol Biomarkers Prev* 2008;17:1411–1417.
234. Gescher A, Steward WP, Brown K. Resveratrol in the management of human cancer: how strong is the clinical evidence? *Ann N Y Acad Sci* 2013;1290:12–20.
235. Stoner GD. Ginger: is it ready for prime time? *Cancer Prev Res (Phila)* 2013;6:257–262.
236. Stoner GD, Wang LS. Chemoprevention of esophageal squamous cell carcinoma with berries. *Top Curr Chem* 2013;329:1–20.
237. Mallery SR, Zwick JC, Pei P, et al. Topical application of a bioadhesive black raspberry gel modulates gene expression and reduces cyclooxygenase 2 protein in human premalignant oral lesions. *Cancer Res* 2008;68:4945–4957.
238. Carroll RE, Benya RV, Turgeon DK, et al. Phase IIa clinical trial of curcumin for the prevention of colorectal neoplasia. *Cancer Prev Res (Phila)* 2011;4:354–364.
239. Seeff LB, Hoofnagle JH. Epidemiology of hepatocellular carcinoma in areas of low hepatitis B and hepatitis C endemicity. *Oncogene* 2006;25:3771–3777.
240. Fox JG, Wang TC. Inflammation, atrophy, and gastric cancer. *J Clin Invest* 2007;117:60–69.
241. Saslow D, Castle PE, Cox JT, et al. American Cancer Society Guideline for human papillomavirus (HPV) vaccine use to prevent cervical cancer and its precursors. *CA Cancer J Clin* 2007;57:7–28.

242. Mohanna S, Maco V, Bravo F, et al. Epidemiology and clinical characteristics of classic Kaposi's sarcoma, seroprevalence, and variants of human herpesvirus 8 in South America: a critical review of an old disease. *Int J Infect Dis* 2005;9:239–250.
243. Castillo JJ, Reagan JL, Bishop KD, et al. Viral lymphomagenesis: from pathophysiology to the rationale for novel therapies. *Br J Haematol* 2014;165:300–315.
244. Al-Bahrani R, Abuetaf Y, Zeitouni N, et al. Cholangiocarcinoma: risk factors, environmental influences and oncogenesis. *Ann Clin Lab Sci* 2013;43:195–210.
245. Mostafa MH, Sheweita SA, O'Connor PJ. Relationship between schistosomiasis and bladder cancer. *Clin Microbiol Rev* 1999;12:97–111.
246. Zivny J, Wang TC, Yantiss R, et al. Role of therapy or monitoring in preventing progression to gastric cancer. *J Clin Gastroenterol* 2003;36:S50–S60.
247. Correa P, Fontham ET, Bravo JC, et al. Chemoprevention of gastric dysplasia: randomized trial of antioxidant supplements and anti-helicobacter pylori therapy. *J Natl Cancer Inst* 2000;92:1881–1888.
248. Wong BC, Zhang L, Ma JL, et al. Effects of selective COX-2 inhibitor and Helicobacter pylori eradication on precancerous gastric lesions. *Gut* 2012;61:812–818.
249. Ma JL, Zhang L, Brown LM, et al. Fifteen-year effects of Helicobacter pylori, garlic, and vitamin treatments on gastric cancer incidence and mortality. *J Natl Cancer Inst* 2012;104:488–492.
250. Risch HA, Lu L, Kidd MS, et al. Helicobacter pylori seropositivities and risk of pancreatic carcinoma. *Cancer Epidemiol Biomarkers Prev* 2014;23:172–178.
251. Mazzoleni LE, Francesconi CF, Sander GB. Mass eradication of *Helicobacter pylori*: feasible and advisable? *Lancet* 2011;378:462–464.
252. Whiteman DC, Parmar P, Fahey P, et al. Association of Helicobacter pylori infection with reduced risk for esophageal cancer is independent of environmental and genetic modifiers. *Gastroenterology* 2010;139:73–83.
253. Torrance CJ, Jackson PE, Montgomery E, et al. Combinatorial chemoprevention of intestinal neoplasia. *Nat Med* 2000;6:1024–1028.
254. Reddy BS, Wang CX, Kong AN, et al. Prevention of azoxymethane-induced colon cancer by combination of low doses of atorvastatin, aspirin, and celecoxib in F 344 rats. *Cancer Res* 2006;66:4542–4546.
255. Zell JA, Pelot D, Chen WP, et al. Risk of cardiovascular events in a randomized placebo-controlled, double-blind trial of difluoromethylornithine plus sulindac for the prevention of sporadic colorectal adenomas. *Cancer Prev Res (Phila)* 2009;2:209–212.
256. Guerrieri-Gonzaga A, Robertson C, Bonanni B, et al. Preliminary results on safety and activity of a randomized, double-blind, 2 x 2 trial of low-dose tamoxifen and fenretinide for breast cancer prevention in premenopausal women. *J Clin Oncol* 2006;24:129–135.
257. Kelloff GJ, Lippman SM, Dannenberg AJ, et al. Progress in chemoprevention drug development: the promise of molecular biomarkers for prevention of intraepithelial neoplasia and cancer—a plan to move forward. *Clin Cancer Res* 2006;12:3661–3697.
258. Washington MK, Powell AE, Sullivan R, et al. Pathology of rodent models of intestinal cancer: progress report and recommendations. *Gastroenterology* 2013;144:705–717.
259. Nandan MO, Yang VW. Genetic and chemical models of colorectal cancer in mice. *Curr Colorectal Cancer Rep* 2010;6:51–59.
260. Kwon MC, Berns A. Mouse models for lung cancer. *Mol Oncol* 2013;7:165–177.
261. Kirma NB, Tekmal RR. Transgenic mouse models of hormonal mammary carcinogenesis: advantages and limitations. *J Steroid Biochem Mol Biol* 2012;131:76–82.
262. Irshad S, Abate-Shen C. Modeling prostate cancer in mice: something old, something new, something premalignant, something metastatic. *Cancer Metastasis Rev* 2013;32:109–122.
263. Herreros-Villanueva M, Hijona E, Cosme A, et al. Mouse models of pancreatic cancer. *World J Gastroenterol* 2012;18:1286–1294.
264. Winawer SJ, Zaubler AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. *N Engl J Med* 1993;329:1977–1981.
265. Spechler S. Barrett's esophagus. *Semin Oncol* 1994;21:431–437.
266. Shen O, Liu S, Dawsey S, et al. Cytologic screening for esophageal cancer: results from 12,877 subjects from a high risk population in China. *Int J Cancer* 1993;54:185–188.
267. Taylor P, Li B, Dawsey S, et al. Prevention of esophageal cancer: the nutrition intervention trials in Linxian, China. Linxian Nutrition Intervention Trials Study Group. *Cancer Res* 1994;54:2029s–2031s.
268. Sober A, Burstein J. Precursors to skin cancer. *Cancer* 1995;75:645–650.
269. Tucker M, Halpern A, Holly E, et al. Clinically recognized dysplastic nevi. A central risk factor for cutaneous melanoma. *JAMA* 1997;277:1439–1444.
270. Gustafsson L, Adami H-O. Natural history of cervical neoplasia: consistent results obtained by an identification technique. *Br J Cancer* 1989;60:132–137.
271. Cawson R. Premalignant lesions in the mouth. *Br Med Bull* 1975;31:164–180.
272. Zhou M. Intraductal carcinoma of the prostate: the whole story. *Pathology* 2013;45:533–539.
273. Saccomanno G, Archer VE, Auerbach O, et al. Development of carcinoma of the lung as reflected in exfoliated cells. *Cancer* 1974;33:256–270.
274. Cooper CL, O'Toole SA, Kench JG. Classification, morphology and molecular pathology of premalignant lesions of the pancreas. *Pathology* 2013;45:286–304.
275. Brewster AM, Lee JJ, Clayman GL, et al. Randomized trial of adjuvant 13-cis-retinoic acid and interferon alfa for patients with aggressive skin squamous cell carcinoma. *J Clin Oncol* 2007;25:1974–1978.
276. Karp DD, Lee SJ, Keller SM, et al. Randomized, double-blind, placebo-controlled, phase III chemoprevention trial of selenium supplementation in patients with resected stage I non-small-cell lung cancer: ECOG 5597. *J Clin Oncol* 2013;31:4179–4187.
277. Labayle D, Fischer D, Vielh P. Sulindac causes regression of rectal polyps in familial adenomatous polyposis. *Gastroenterology* 1991;101:635–639.
278. Giardiello FM, Hamilton SR, Krush AJ, et al. Treatment of colonic and rectal adenomas with sulindac in familial adenomatous polyposis. *N Engl J Med* 1993;328:1313–1316.
279. Nugent KP, Farmer KC, Sippelman AD, et al. Randomized controlled trial of the effect of sulindac on duodenal and rectal polyposis and cell proliferation in patients with familial adenomatous polyposis. *Br J Surg* 1993;80:1618–1619.
280. Mathers JC, Movahedi M, Macrae F, et al. Long-term effect of resistant starch on cancer risk in carriers of hereditary colorectal cancer: an analysis from the CAPP2 randomised controlled trial. *Lancet Oncol* 2012;13:1242–1249.
281. Burn J, Gerdes AM, Macrae F, et al. Long-term effect of aspirin on cancer risk in carriers of hereditary colorectal cancer: an analysis from the CAPP2 randomised controlled trial. *Lancet* 2011;378:2081–2087.
282. Ruffin MT, Krishnan K, Rock CL, et al. Suppression of human colorectal mucosal prostaglandins: determining the lowest effective aspirin dose. *J Natl Cancer Inst* 1997;89:1152–1160.
283. Krishnan K, Ruffin MT, Normolle D, et al. Colonic mucosal prostaglandin E2 and cyclooxygenase expression before and after low aspirin doses in subjects at high risk or at normal risk for colorectal cancer. *Cancer Epidemiol Biomarkers Prev* 2001;10:447–453.
284. Sample D, Wargovich M, Fischer SM, et al. A dose-finding study of aspirin for chemoprevention utilizing rectal mucosal prostaglandin E(2) levels as a biomarker. *Cancer Epidemiol Biomarkers Prev* 2002;11:275–279.
285. Sandler RS, Halabi S, Baron JA, et al. A randomized trial of aspirin to prevent colorectal adenomas in patients with previous colorectal cancer. *N Engl J Med* 2003;348:883–890.
286. Baron JA, Cole BF, Sandler RS, et al. A randomized trial of aspirin to prevent colorectal adenomas. *N Engl J Med* 2003;348:891–899.
287. Fisher B, Costantino JP, Wickerham DL, et al. Tamoxifen for the prevention of breast cancer: current status of the National Surgical Adjuvant Breast and Bowel Project P-1 study. *J Natl Cancer Inst* 2005;97:1652–1662.
288. Cuzick J, Forbes JF, Sestak I, et al. Long-term results of tamoxifen prophylaxis for breast cancer—96-month follow-up of the randomized IBIS-I trial. *J Natl Cancer Inst* 2007;99:272–282.
289. Powles TJ, Ashley S, Tidy A, et al. Twenty-year follow-up of the Royal Marsden randomized, double-blinded tamoxifen breast cancer prevention trial. *J Natl Cancer Inst* 2007;99:283–290.
290. Veronesi U, Maisonneuve P, Rotmensz N, et al. Tamoxifen for the prevention of breast cancer: Late results of the Italian randomized tamoxifen prevention trial among women with hysterectomy. *J Natl Cancer Inst* 2007;99:727–737.
291. Cauley JA, Norton L, Lippman ME, et al. Continued breast cancer risk reduction in postmenopausal women treated with raloxifene: 4-year results from the MORE trial. Multiple outcomes of raloxifene evaluation. *Breast Cancer Res Treat* 2001;65:125–134.
292. Martino S, Cauley JA, Barrett-Connor E, et al. Continuing outcomes relevant to Evista: breast cancer incidence in postmenopausal osteoporotic women in a randomized trial of raloxifene. *J Natl Cancer Inst* 2004;96:1751–1761.
293. Messing E, Kim KM, Sharkey F, et al. Randomized prospective phase III trial of difluoromethylornithine vs placebo in preventing recurrence of completely resected low risk superficial bladder cancer. *J Urol* 2006;176:500–504.
294. Simoneau AR, Cerner EW, Nagle R, et al. The effect of difluoromethylornithine on decreasing prostate size and polyamines in men: results of a year-long phase IIb randomized placebo-controlled chemoprevention trial. *Cancer Epidemiol Biomarkers Prev* 2008;17:292–299.
295. Bailey HH, Kim K, Verma AK, et al. A randomized, double-blind, placebo-controlled phase 3 skin cancer prevention study of [alpha]-difluoromethylornithine in subjects with previous history of skin cancer. *Cancer Prev Res (Phila)* 2010;3:35–47.
296. Kreul SM, Havighurst T, Kim K, et al. A phase III skin cancer chemoprevention study of DFMO: long-term follow-up of skin cancer events and toxicity. *Cancer Prev Res (Phila)* 2012;5:1368–1374.
297. Zick SM, Ruffin MT, Djuric Z, et al. Quantitation of 6-, 8- and 10-gingerols and 6-shogaol in human plasma by high-performance liquid chromatography with electrochemical detection. *Int J Biomed Sci* 2010;6:233–240.
298. Zick SM, Turgeon DK, Vared SK, et al. Phase II study of the effects of ginger root extract on eicosanoids in colon mucosa in people at normal risk for colorectal cancer. *Cancer Prev Res (Phila)* 2011;4:1929–1937.
299. Hull MA. Nutritional agents with anti-inflammatory properties in chemoprevention of colorectal neoplasia. *Recent Results Cancer Res* 2013;191:143–156.
300. Nelson WG, De Marzo AM, Isaacs WB. Prostate cancer. *N Engl J Med* 2003;349:366–381.

301. von Knobloch R, Konrad L, Barth PJ, et al. Genetic pathways and new progression markers for prostate cancer suggested by microsatellite allelotyping. *Clin Cancer Res* 2004;10:1064–1073.
302. Palapattu GS, Sutcliffe S, Bastian PJ, et al. Prostate carcinogenesis and inflammation: emerging insights. *Carcinogenesis* 2005;26:1170–1181.
303. Dontu G, Liu S, Wicha MS. Stem cells in mammary development and carcinogenesis: implications for prevention and treatment. *Stem Cell Rev* 2005;1:207–213.
304. Liu S, Dontu G, Mantle ID, et al. Hedgehog signaling and Bmi-1 regulate self-renewal of normal and malignant human mammary stem cells. *Cancer Res* 2006;66:6063–6071.
305. Wistuba II, Lam S, Behrens C, et al. Molecular damage in the bronchial epithelium of current and former smokers. *J Natl Cancer Inst* 1997;89:1366–1373.
306. Massion PP, Carbone DP. The molecular basis of lung cancer: molecular abnormalities and therapeutic implications. *Respir Res* 2003;4:12.
307. Mao C, Koutsky LA, Ault KA, et al. Efficacy of human papillomavirus-16 vaccine to prevent cervical intraepithelial neoplasia: a randomized controlled trial. *Obstet Gynecol* 2006;107:18–27.
308. Califano J, van der Riet P, Westra W, et al. Genetic progression model for head and neck cancer: implications for field cancerization. *Cancer Res* 1996;56:2488–2492.
309. Califano J, Westra WH, Meininger G, et al. Genetic progression and clonal relationship of recurrent premalignant head and neck lesions. *Clin Cancer Res* 2000;6:347–352.
310. Braakhuis BJ, Tabor MP, Kummer JA, et al. A genetic explanation of Slaughter's concept of field cancerization: evidence and clinical implications. *Cancer Res* 2003;63:1727–1730.
311. Ha PK, Benoit NE, Yochem R, et al. A transcriptional progression model for head and neck cancer. *Clin Cancer Res* 2003;9:3058–3064.
312. Barrett MT, Sanchez CA, Prevo LJ, et al. Evolution of neoplastic cell lineages in Barrett oesophagus. *Nat Genet* 1999;22:106–109.
313. Reid BJ, Levine DS, Longton G, et al. Predictors of progression to cancer in Barrett's esophagus: baseline histology and flow cytometry identify low- and high-risk patient subsets. *Am J Gastroenterol* 2000;95:1669–1676.
314. Thorgeirsson SS, Grisham JW. Molecular pathogenesis of human hepatocellular carcinoma. *Nat Genet* 2002;31:339–346.