

REFERENCES

1. Parkin, D.M., et al., Global cancer statistics, 2002. *CA Cancer J Clin*, 2005. **55**(2): p. 74-108.
2. Martinez, M.E., Primary prevention of colorectal cancer: lifestyle, nutrition, exercise. *Recent Results Cancer Res*, 2005. **166**: p. 177-211.
3. Chyou, P.H., A.M. Nomura, and G.N. Stemmermann, A prospective study of colon and rectal cancer among Hawaii Japanese men. *Ann Epidemiol*, 1996. **6**(4): p. 276-82.
4. South Australian Cancer Registry, E.B., Cancer in South Australia 2002 *Government of South Australia, Department of Health*, February 2005.
5. Australian federal government, D.o.h.a.a., *Investing in Australia's health: Strengthening cancer care*, in *Budget 2005-2006 Health 1*. 10 May 2005.
6. Young, G.P. and S. Cole, New stool screening tests for colorectal cancer. *Digestion*, 2007. **76**(1): p. 26-33.
7. Trowbridge, B. and R.W. Burt, Colorectal cancer screening. *Surg Clin North Am*, 2002. **82**(5): p. 943-57.
8. Stewart, B.W. and P. Kleihues, *World cancer report. 2007*: IARC Press.
9. Topping, D.L. and P.M. Clifton, Short-chain fatty acids and human colonic function: Roles of resistant starch and nonstarch polysaccharides. *Physiological reviews*, 2001. **81**(3): p. 1031-1064.
10. McIntyre, A., P.R. Gibson, and G.P. Young, Butyrate production from dietary fibre and protection against large bowel cancer in a rat model. *Gut*, 1993. **34**: p. 386-391.
11. Le Leu, R.K., et al., Suppression of azoxymethane-induced colon cancer development in rats by dietary resistant starch. *Cancer Biol Ther*, 2007. **6**(10): p. 1621-6.
12. Matthews, G.M., G.S. Howarth, and R.N. Butler, Short-Chain Fatty Acid Modulation of Apoptosis in the Kato III Human Gastric Carcinoma Cell Line. *Cancer Biol Ther*, 2007. **6**(7).
13. Le Leu, R.K., et al., Effect of resistant starch on genotoxin-induced apoptosis, colonic epithelium, and luminal contents in rats. *Carcinogenesis*, 2003. **24**(8): p. 1347-52.

14. Potter, J.D. and K. Steinmetz, Vegetables, fruit and phytoestrogens as preventive agents. *IARC Sci Publ*, 1996(139): p. 61-90.
15. *World Cancer Report*, ed. B.W. Stewart and P. Kleihues. 2003: IARC Press.
16. Rose, D.P., Dietary fatty acids and cancer. *American Journal of Clinical Nutrition*, 1997. **66**: p. 998S-1003S.
17. English, D.R., et al., Red meat, chicken and fish consumption and risk of colorectal cancer. *Cancer Epidemiol Biomarkers Prev*, 2004. **13**: p. 1509-1514.
18. Flood, A., et al., Meat, fat and their subtyores as risk factors for colorectal cancer in a prosective cohort of women. *Am J Epidiemiol*, 2003. **158**: p. 59-68.
19. Turesky, R.J., Formation and biochemistry of carcinogenic heterocyclic aromatic amines in cooked meats. *Toxicol Lett*, 2007. **168**(3): p. 219-27.
20. Lewin, M.H., et al., Red meat enhances the colonic formation of the DNA adduct O6-carboxymethyl guanine: implications for colorectal cancer risk. *Cancer Res*, 2006. **66**(3): p. 1859-65.
21. Kuhnle, G.G. and S.A. Bingham, Dietary meat, endogenous nitrosation and colorectal cancer. *Biochem Soc Trans*, 2007. **35**(Pt 5): p. 1355-7.
22. Lunn, J.C., et al., The effect of haem in red and processed meat on the endogenous formation of N-nitroso compounds in the upper gastrointestinal tract. *Carcinogenesis*, 2007. **28**(3): p. 685-90.
23. Lichtenstein, A.H., et al., Dietary fat consumption and health. *Nutrition Reviews*, 1998. **56**(5.2): p. S3-26.
24. Nkondjock, A., et al., Specific fatty acids and human colorectal cancer: an overview. *Cancer Detect Prev*, 2003. **27**(1): p. 55-66.
25. Simopoulos, A.P., The importance of the ratio of omega-6/omega-3 essential fatty acids. *Biomed Pharmacother*, 2002. **56**(8): p. 365-79.
26. Bang, H.O., J. Dyerberg, and N. Hjerne, The composition of food consumed by Greenland Eskimos. *Acta Med Scand*, 1976. **200**: p. 69--73.
27. Kromann, N. and A. Green, Epidemiological studies in the Upernavik District, Greenland: incidence of some chronic diseases (1950-1974). *Acta Med Scand*, 1980. **208**(401-6).

28. Karam, S.M., Lineage commitment and maturation of epithelial cells in the gut. *Front Biosci*, 1999. **4**: p. D286-98.
29. Boland, R.C., *Neoplasia of the Gastrointestinal tract*, in *Textbook of Gastroenterology*, T. Yamada, Editor. 1995, JB Lippincott Company: Philadelphia. p. 578 - 595.
30. Bird, A.R., Role of aberrant crypt foci in understanding the pathogenesis of colorectal cancer. *Cancer Letters*, 1995. **93**(1): p. 55-71.
31. Shinya, H. and W.I. Wolff, Morphology, anatomic distribution and cancer potential of colonic polyps. *Ann Surg*, 1979. **190**(6): p. 679-683.
32. Jessup, J.M. and G.E. Gallick, The biology of colorectal carcinoma. *Curr Probl Cancer*, 1992. **16**(5): p. 261-328.
33. Malumbres, M. and M. Barbacid, RAS oncogenes: the first 30 years. *Nat Rev Cancer*, 2003. **3**(6): p. 459-65.
34. Adjei, A.A., Blocking oncogenic Ras signaling for cancer therapy. *J Natl Cancer Inst*, 2001. **93**(14): p. 1062-74.
35. Sancar, A., et al., Molecular mechanisms of mammalian DNA repair and the DNA damage checkpoints. *Annu Rev Biochem*, 2004. **73**: p. 39-85.
36. Konishi, M., Molecular nature of colon tumours in hereditary nonpolyposis colon cancer, familial polyposis and sporadic colon cancer. *Gastroenterology*, 1996. **111**(2): p. 307-317.
37. Suzuki, K., et al., Global DNA demethylation in gastrointestinal cancer is age dependent and precedes genomic damage. *Cancer cell*, 2006. **9**(3): p. 199-207.
38. Toyota, M., et al., DNA methylation changes in gastrointestinal disease. *Journal of Gastroenterology*, 2002. **37**(14): p. 97-101.
39. Powell, S.M., N. Zilz, and Y. Beazer-Barclay, APC mutations occur early during colorectal tumorigenesis. *Nature*, 1992. **359**: p. 235-7.
40. Cardini, G., D. DeFillipo, and C. Luceri, APC mutations in aberrant crypt foci and colonic tumours induced by aoxymethane in rats. *Proceedings of the American Association for Cancer Research*, 1997. **38**: p. 467.
41. Shivapurkar, N., L. Huang, and B. Ruggeri, K-ras and p53 mutations in aberrant crypt foci and colonic tumors from colon cancer patients. *Cancer letters*, 1997. **115**(1): p. 39-46.

42. Yuan, P., M.H. Sun, and J.S. hang, APC and K-ras gene mutation in aberrant crypt foci of human colon. *World J Gastroenterol*, 2001. **7**(3): p. 352-6.
43. Lynch, H.T. and A. De la Chapelle, Hereditary colorectal cancer. *N Engl J Med*, 2003. **348**: p. 919-932.
44. Sharma, R.A. and P.B. Farmer, Biological relevance of adduct detection to the chemoprevention of cancer. *Clin Cancer Res*, 2004. **10**(15): p. 4901-12.
45. Povey, A.C., DNA adducts: endogenous and induced. *Toxicol Pathol*, 2000. **28**(3): p. 405-14.
46. Farmer, P.B., DNA and protein adducts as markers of genotoxicity. *Toxicol Lett*, 2004. **149**(1-3): p. 3-9.
47. Marnett, L.J., Oxyradicals and DNA damage. *Carcinogenesis*, 2000. **21**(3): p. 361-70.
48. Chung, F.L., H.J. Chen, and R.G. Nath, Lipid peroxidation as a potential endogenous source for the formation of exocyclic DNA adducts. *Carcinogenesis*, 1996. **17**(10): p. 2105-11.
49. Margison, G.P., M.F. Santibanez Koref, and A.C. Povey, Mechanisms of carcinogenicity/chemotherapy by O6-methylguanine. *Mutagenesis*, 2002. **17**(6): p. 483-7.
50. Margison, G.P. and P.J. O'Connor, *Biological consequences of reactions with DNA: Role of specific Lesions*, in *Chemical carcinogenesis and mutagenesis*, P. Grover and D. Phillips, Editors. 1990: Heidelberg, Germany. p. 547-571.
51. Nehls, P. and M.F. Rajewsky, Ethylation of nucleophilic sites in DNA by N-ethyl-N-nitrosourea depends on chromatin structure and ionic strength. *Mutation Research*, 1985. **150**: p. 13-21.
52. Sendowski, K. and M.F. Rajewsky, DNA sequence dependence of guanine-O⁶ alkylation by the N-nitroso carcinogens N-methyl and N-ethyl-N-nitrosourea. *Mutation Research*, 1991. **250**: p. 153-160.
53. Yamagata, Y., K. Kohda, and K. Tomita, Structural studies of O6-methyldeoxyguanosine and related compounds: a promutagenic DNA lesion by methylating carcinogens. *Nucleic Acids Res*, 1988. **16**(19): p. 9307-21.

54. Margison, G.P. and P.J. O'Connor, *Nucleic acid modification by N-nitroso compounds*, in *Chemical carcinogens and DNA*. 1979, CRC Press, Boca Ranton: Florida. p. 111-150.
55. Abbott, P.J. and R. Saffhill, DNA synthesis with methylated poly(dC-dG) templates. Evidence for a competitive nature to miscoding by O6-methylguanine. *Biochem Biophys Acta*, 1979. **562**: p. 51-61.
56. Richardson, K.K., et al., DNA base changes induced following in vivo exposure of unadapted, adapted or Ada *Escherichia coli* to N-methyl-N-nitro-N-nitrosoguanidine. *Mol. Gen. Genet.*, 1987. **209**: p. 526-532.
57. Burns, P.A., A.J. Gordon, and B.W. Glickman, Influence of neighbouring base sequence on N-methyl-N-nitro-N-nitrosoguanidine mutagenesis in the lacI gene of *Escherichia coli*. *J. Mol. Biol.*, 1987. **194**(3): p. 385-390.
58. Povey, A.C., et al., Elevated levels of the pro-carcinogenic adduct, O(6)-methylguanine, in normal DNA from the cancer prone regions of the large bowel. *Gut*, 2000. **47**(3): p. 362-5.
59. Rao, C.V., J. Nayini, and B.S. Reddy, Effect of oltipraz [5-(2-pyrazinyl)-4-methyl-1,2-dithiol-3-thione] on azoxymethane-induced biochemical changes related to early colon carcinogenesis in male F344 rats. *Proc Soc Exp Biol Med*, 1991. **197**(1): p. 77-84.
60. Jackson, P.E., et al., Associations between tissue-specific DNA alkylation, DNA repair and cell proliferation in the colon and colon tumour yield in mice treated with 1,2-dimethylhydrazine. *Carcinogenesis*, 2003. **24**(3): p. 527-33.
61. Hong, M.Y., et al., Relationship between DNA adduct levels, repair enzyme, and apoptosis as a function of DNA methylation by azoxymethane. *Cell Growth Differ*, 1999. **10**(11): p. 749-58.
62. Barch, D.H. and C.C. Fox, Dietary zinc deficiency increases the methylbenzyl nitrosamine-induced formation of O6-methylguanine in the esophageal DNA of the rat. *Carcinogenesis*, 1987. **8**(10): p. 1461-4.
63. Tacchi-Bedford, A.M., G.D. Whyman, and A.E. McLean, DNA alkylation by 1,2-dimethylhydrazine in the rat large intestine and liver: influence of diet and enzyme induction. *Toxicology*, 1988. **50**(2): p. 181-91.

64. Jacoby, R.F., et al., Supplemental dietary calcium fails to alter the acute effects of 1,2-dimethylhydrazine on O6-methylguanine, O6-alkylguanine-DNA alkyltransferase and cellular proliferation in the rat colon. *Carcinogenesis*, 1993. **14**(6): p. 1175-9.
65. Shimpo, K., et al., Inhibition of azoxymethane-induced DNA adduct formation by *Aloe arborescens* var. *natalensis*. *Asian Pac J Cancer Prev*, 2003. **4**(3): p. 247-51.
66. Suaeyun, R., et al., Inhibitory effects of lemon grass (*Cymbopogon citratus* Stapf) on formation of azoxymethane-induced DNA adducts and aberrant crypt foci in the rat colon. *Carcinogenesis*, 1997. **18**(5): p. 949-55.
67. Prokopczyk, B., et al., Effects of dietary 1,4-phenylenebis(methylene)selenocyanate on 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone-induced DNA adduct formation in lung and liver of A/J mice and F344 rats. *Carcinogenesis*, 1996. **17**(4): p. 749-53.
68. el-Bayoumy, K., et al., Effects of dietary fat content on the metabolism of NNK and on DNA methylation induced by NNK. *Nutr Cancer*, 1996. **26**(1): p. 1-10.
69. Hong, M.Y., et al., Dietary fish oil reduces O6-methylguanine DNA adduct levels in rat colon in part by increasing apoptosis during tumor initiation. *Cancer Epidemiol Biomarkers Prev*, 2000. **9**(8): p. 819-26.
70. Hall, P.A., et al., Regulation of cell number in the mammalian gastrointestinal tract: the importance of apoptosis. *Journal of Cell Science*, 1994. **107**(3569-3577).
71. Huerta, S., E.J. Goulet, and E.H. Livingston, Colon cancer and apoptosis. *Am J Surg*, 2006. **191**(4): p. 517-26.
72. Lane, D.P., p53 guardian of the genome. *Nature*, 1992. **358**: p. 15-16.
73. Miyashita, T. and J.C. Reed, Tumor suppressor p53 is a direct transcriptional activator of the human *bax* gene. *Cell* 1995. **80**: p. 293-299.
74. Mosner, J., T. Mummenbrauer, and C. Bauer, Negative feed-back regulation of wild type p53 biosynthesis. *EMBO J*, 1995. **14**(4442-4449).
75. Korsmeyer, S.J., BCL-2 gene family and the regulation of programmed cell death. *Cancer research*, 1999. **59**(7): p. 1693s-1700s.

76. Potten, C.S., The significance of spontaneous of induced apoptosis in the gastrointestinal tract of mice. *Cancer Metastasis Rev*, 1992. **11**: p. 179-195.
77. Hu, Y., et al., The colonic response to genotoxic carcinogens in the rat: regulation by dietary fibre. *Carcinogenesis*, 2002. **23**(7): p. 1131-7.
78. Gerson, S.L., MGMT: its role in cancer aetiology and cancer therapeutics. *Nat Rev Cancer*, 2004. **4**(4): p. 296-307.
79. Ishibashi, T., et al., Intracellular localisation and function of DNA repair methyltransferase in human cells. *Mutat Res*, 1994. **315**: p. 199-212.
80. Tsuzuki, T., et al., Targeted disruption of the DNA repair methyltransferase gene renders mice hypersensitive to alkylating agent. *Carcinogenesis*, 1996. **17**(6): p. 1215-20.
81. Glassner, B.J., et al., DNA repair methyltransferase (Mgmt) knockout mice are sensitive to the lethal effects of chemotherapeutic alkylating agents. *Mutagenesis*, 1999. **14**(3): p. 339-47.
82. Shiraishi, A., K. Sakumi, and M. Sekiguchi, Increased susceptibility to chemotherapeutic alkylating agents of mice deficient in DNA repair methyltransferase. *Carcinogenesis*, 2000. **21**(10): p. 1879-83.
83. Wali, R.K., et al., Inhibition of O(6)-methylguanine-DNA methyltransferase increases azoxymethane-induced colonic tumors in rats. *Carcinogenesis*, 1999. **20**(12): p. 2355-60.
84. Zaidi, N.H., L. Liu, and S.L. Gerson, Quantitative immunohistochemical estimates of O6-alkylguanine-DNA alkyltransferase expression in normal and malignant human colon. *Clin Cancer Res*, 1996. **2**(3): p. 577-84.
85. Margison, G.P., et al., Variability and regulation of O6-alkylguanine-DNA alkyltransferase. *Carcinogenesis*, 2003. **24**(4): p. 625-35.
86. O'Connor, T.R. and J. Laval, Human cDNA expressing a functional DNA glycosylase excising 3-methyladenine and 7-methylguanine. *Biochem Biophys Res Commun*, 1991. **176**: p. 1170-1177.
87. Hitomi, K., S. Iwai, and J. Tainer, The intricate structural chemistry of base excision repair machinery; Implications for DNA damage recognition, removal and repair. *DNA repair*, 2007. **6**: p. 410-428.
88. Fishel, R., Mismatch repair, molecular switches and signal transduction. *Genes Dev*, 1998. **12**: p. 2096-2101.

89. Modrich, P. and R. Lahue, Mismatch repair in replication fidelity, genetic recombination and cancer biology. *Ann Rev Biochem*, 1996. **65**: p. 101-133.
90. Bellacosa, A., Functional interactions and signaling properties of mammalian DNA mismatch repair. *Cell Death Differ*, 2001. **8**: p. 1049-1051.
91. Schofield, M.J. and P. Hsieh, DNA mismatch repair: molecular mechanisms and biological function. *Ann Rev Microbiol*, 2003. **57**: p. 579-608.
92. Bignami, M., I. Casorelli, and P. Karran, 2003. *Eur J Cancer*, Mismatch repair and response to DNA-damaging antitumour therapies. **39**: p. 2142-2149.
93. Gradia, S., et al., hMSH2-hMSH6 forms a hydrolysis-independent sliding clamp on mismatched DNA. *Mol Cell*, 1999. **3**: p. 255-261.
94. Li, G.M. and P. Modrich, Restoration of mismatch repair to nuclear extracts of H6 colorectal tumour cells by a heterodimer of human MutL homologs. *Proc Natl Acad Sci U S A*, 1995. **92**: p. 1950-1954.
95. Kaina, B., DNA damage-triggered apoptosis: critical role of DNA repair, double-strand breaks, cell proliferation and signaling. *Biochem Pharmacol*, 2003. **66**(8): p. 1547-54.
96. Meikrantz, W., et al., O6-alkylguanine DNA lesions trigger apoptosis. *Carcinogenesis*, 1998. **19**(2): p. 369-72.
97. Ochs, K. and B. Kaina, Apoptosis induced by DNA damage O6-methylguanine is Bcl-2 and caspase-9/3 regulated and Fas/caspase-8 independent. *Cancer Res*, 2000. **60**(20): p. 5815-24.
98. Roos, W.P. and B. Kaina, DNA damage-induced cell death by apoptosis. *Trends Mol Med*, 2006. **12**(9): p. 440-50.
99. Fishel, R., et al., The human mutator gene homolog MSH2 and its association with hereditary nonpolyposis colon cancer. *Cell*, 1993. **75**(1027-1038).
100. Bronner, C.E., et al., Mutation in the DNA mismatch repair gene homologue hMLH1 is associated with hereditary non-polyposis colon cancer. *Nature*, 1994. **368**: p. 258-261.

101. McCowen, K.C. and B.R. Bistrain, Essential fatty acids and their derivatives. *Curr Opin Gastroenterol*, 2005. **21**(2): p. 207-15.
102. Cohen, Z., H.A. Norman, and Y.M. Heimer, Microalgae a source of omega3 fatty acids. *Plants in human nutrition*, 1995(77).
103. Caygill, C.P., A. Charlett, and M.J. Hill, Fat, fish, fish oil and cancer. *Br J Cancer*, 1996. **74**(1): p. 159-64.
104. Calder, P.C. and R.F. Grimble, Polyunsaturated fatty acids, inflammation and immunity. *Eur J Clin. Nutr.*, 2002. **56**: p. s14-19.
105. Rose, D.P. and J.M. Connolly, Omega-3 fatty acids as cancer chemopreventive agents. *Pharmacol Ther*, 1999. **83**: p. 217-244.
106. Whelan, J. and M.F. McEntee, Dietary (n-6) PUFA and intestinal tumorigenesis. *J Nutr*, 2004. **134**(12 Suppl): p. 3421S-3426S.
107. Crawford, M., et al., Role of plant derived omega-3 fatty acids in human nutrition. *Ann Nutr Metab.* **44**, 2000. **263-5**.
108. Willett, W.C., W. Smalley, and R. DuBois, Aspirin use and potential mechanisms for colorectal cancer prevention. *J Clin Invest*, 1997. **100**(6): p. 1325-9.
109. C., G.-S., L. I, and H. O, Cyclooxygenase-1 and cyclooxygenase-2 gene expression in human colorectal adenocarcinomas and in azoxymethane induced colonic tumours in rats. *Gut*, 1996. **38**(1): p. 79-84.
110. Hamid, R., et al., Inhibition by dietary menhaden oil of cyclooxygenase-1 and 2 in N-nitrosomethylurea induced rat mammary tumors. *Int J Oncol*, 1999. **14**: p. 523-8.
111. Reddy, B.S., et al., Prevention of colon cancer by low doses of celecoxib, a cyclooxygenase inhibitor, administered in diet rich in omega-3 polyunsaturated fatty acids. *Cancer Res*, 2005. **65**(17): p. 8022-7.
112. Swamy, M.V., et al., Modulation of cyclooxygenase-2 activities by the combined action of celecoxib and decosahexaenoic acid: novel strategies for colon cancer prevention and treatment. *Mol Cancer Ther*, 2004. **3**(2): p. 215-21.
113. Dommels, Y.E., et al., The role of cyclooxygenase in n-6 and n-3 polyunsaturated fatty acid mediated effects on cell proliferation, PGE(2) synthesis and cytotoxicity in human colorectal carcinoma cell lines. *Carcinogenesis*, 2003. **24**(3): p. 385-92.

114. Narayanan, B.A., N.K. Narayanan, and B.S. Reddy, Docosahexaenoic acid regulated genes and transcription factors inducing apoptosis in human colon cancer cells. *Int J Oncol*, 2001. **19**(6): p. 1255-62.
115. Vamecq, J. and L. N., Medical significance of peroxisome proliferator activated receptors. *Lancet*, 1999. **354**: p. 141-8.
116. Berger, J. and D.E. Moller, The mechanisms of action of PPARs. *Annu Rev Med*, 2002. **53**: p. 409-35.
117. Novak, T.E., et al., NF-kappa B inhibition by omega-3 fatty acids modulates LPS stimulated macrophage TNF-alpha transcription. *Am J Physiol*, 2003. **284**: p. 84-89.
118. Chen, Z.Y. and N.W. Istfan, Docosahexaenoic acid is a potent inducer of apoptosis in HT-29 colon cancer cells. *Prostaglandins Leukot Essent Fatty Acids*, 2000. **63**(5): p. 301-8.
119. Ng, Y., et al., The role of docosahexaenoic acid in mediating mitochondrial membrane lipid oxidation and apoptosis in colonocytes. *Carcinogenesis*, 2005. **26**(11): p. 1914-21.
120. Chapkin, R.S., et al., Dietary n-3 PUFA alter colonocyte mitochondrial membrane composition and function. *Lipids*, 2002. **37**(2): p. 193-9.
121. Saito, M. and K. Kubo, Relationship between tissue lipid peroxidation and peroxidizability index after alpha-linolenic, eicosapentaenoic, or docosahexaenoic acid intake in rats. *Br J Nutr*, 2003. **89**(1): p. 19-28.
122. Drasar, B. and D. Irving, Environmental factors and cancer of the colon and breast. *Br J Cancer*, 1973. **27**(2): p. 167-72.
123. Jain, M., G. Cook, and F. Davis, A case-control study of diet and colorectal cancer. *Int J Cancer*, 1980. **26**(6): p. 757-68.
124. Haenszel, W., J. Berg, and M. Segi, Large-bowel cancer in Hawaiian Japanese. *J Natl Cancer Inst*, 1973. **51**(6): p. 1765-79
125. Hursting, S.D., M. Thornquist, and M.M. Henderson, Types of dietary fat and the incidence of cancer at five sites. *Prev Med*, 1990. **19**(3): p. 242-53.
126. Busstra, M.C., et al., Tissue Levels of Fish Fatty Acids and Risk of Colorectal Adenomas: a Case-Control Study (Netherlands). *Cancer Causes & Control*. **14**: p. 269-276.

127. Terry, P., et al., No Association Between Fat and Fatty Acids Intake and Risk of Colorectal Cancer. *Cancer Epidemiology, Biomarkers & Prevention*, 2001. **10**.
128. Kobayashi, M., et al., Fish, long-chain n-3 polyunsaturated fatty acids, and risk of colorectal cancer in middle-aged Japanese: the JPHC study. *Nutr Cancer*, 2004. **49**: p. 32-40.
129. Oh, K., et al., Dietary marine n-3 fatty acids in relation to risk of distal colorectal adenoma in women. *Cancer Epidemiol Biomarkers Prev*, 2005. **14**: p. 835-41.
130. Brink, M., et al., Fat and K-Ras Mutations in Sporadic Colorectal Cancer in the Netherlands Cohort Study. *Carcinogenesis*, 2004. **25**: p. 1619-1628
131. Hong, M.Y., et al., Anatomical site-specific response to DNA damage is related to later tumor development in the rat azoxymethane colon carcinogenesis model. *Carcinogenesis*, 2001. **22**(11): p. 1831-5.
132. Hong, M.Y., et al., Fish oil enhances targeted apoptosis during colon tumor initiation in part by downregulating Bcl-2. *Nutr Cancer*, 2003. **46**(1): p. 44-51.
133. Hong, M.Y., et al., Fish oil decreases oxidative DNA damage by enhancing apoptosis in rat colon. *Nutr Cancer*, 2005. **52**(2): p. 166-75.
134. Bancroft, L.K., et al., Dietary fish oil reduces oxidative DNA damage in rat colonocytes. *Free Radic Biol Med*, 2003. **35**(2): p. 149-59.
135. Latham, P., E.K. Lund, and I.T. Johnson, Dietary n-3 PUFA increases the apoptotic response to 1,2-dimethylhydrazine, reduces mitosis and suppresses the induction of carcinogenesis in the rat colon. *Carcinogenesis*, 1999. **20**(4): p. 645-50.
136. Rao, C.V., et al., Modulation of experimental colon tumorigenesis by types and amounts of dietary fatty acids. *Cancer Res*, 2001. **61**(5): p. 1927-33.
137. Dommels, Y.E., et al., Effects of high fat fish oil and high fat corn oil diets on initiation of AOM-induced colonic aberrant crypt foci in male F344 rats. *Food Chem Toxicol*, 2003. **41**(12): p. 1739-47.
138. Coleman, L.J., et al., A diet containing alpha-cellulose and fish oil reduces aberrant crypt foci formation and modulates other possible

- markers for colon cancer risk in azoxymethane-treated rats. *J Nutr*, 2002. **132**(8): p. 2312-8.
139. Reddy, B.S. and H. Maruyama, Effect of dietary fish oil on azoxymethane-induced colon carcinogenesis in male F344 rats. *Cancer Res*, 1986. **46**(7): p. 3367-70.
140. Kim, K.H. and H.S. Park, Dietary supplementation of conjugated linoleic acid reduces colon tumor incidence in DMH-treated rats by increasing apoptosis with modulation of biomarkers. *Nutrition*, 2003. **19**(9): p. 772-7.
141. Zhou, S., et al., Effect of Dietary Fatty Acids on Colon Tumorigenesis Induced by Methyl Nitrosourea in Rats. *Biomedical and Environmental Sciences* 2000. **13**(2): p. 105-116.
142. Singh, J., R. Hamid, and B.S. Reddy, Dietary fish oil inhibits the expression of farnesyl protein transferase and colon tumor development in rodents. *Carcinogenesis*, 1998. **19**(6): p. 985-9.
143. Dwivedi, C., et al., Chemopreventive effects of dietary mustard oil on colon tumor development. *Cancer Lett*, 2003. **196**(1): p. 29-34.
144. Chang, W.L., R.S. Chapkin, and J.R. Lupton, Fish oil blocks azoxymethane-induced rat colon tumorigenesis by increasing cell differentiation and apoptosis rather than decreasing cell proliferation. *J Nutr*, 1998. **128**(3): p. 491-7.
145. Joosun, C. and P. Hyunsuh, Effects of Dietary Fats and Fibers on Modulation of Biomarkers and Tumor Incidence in Rats During 1,2-Dimethylhydrazine-Induced Colon Carcinogenesis. *Nutritional Sciences*, 2001. **4**.
146. Lindner, M.A., A fish oil diet inhibits colon cancer in mice. *Nutr Cancer*, 1991. **15**(1): p. 1-11.
147. Minoura, T., et al., Effect of dietary eicosapentaenoic acid on azoxymethane-induced colon carcinogenesis in rats. *Cancer Res*, 1988. **48**(17): p. 4790-4.
148. Takahashi, M., et al., Effect of docosahexaenoic acid on azoxymethane-induced colon carcinogenesis in rats. *Cancer Lett*, 1994. **83**(1-2): p. 177-84.

149. Takahashi, M., et al., Suppression of azoxymethane-induced rat colon carcinoma development by a fish oil component, docosahexaenoic acid (DHA). *Carcinogenesis*, 1997. **18**(7): p. 1337-42.
150. Hofmanova, J., et al., Interaction of polyunsaturated fatty acids and sodium butyrate during apoptosis in HT-29 human colon adenocarcinoma cells. *Eur J Nutr*, 2005. **44**(1): p. 40-51.
151. Jordan, A. and J. Stein, Effect of an omega-3 fatty acid containing lipid emulsion alone and in combination with 5-fluorouracil (5-FU) on growth of the colon cancer cell line Caco-2. *Eur J Nutr*, 2003. **42**: p. 324-31.
152. Narayanan, B.A., et al., Effects of a combination of docosahexaenoic acid and 1,4-phenylene bis(methylene) selenocyanate on cyclooxygenase 2, inducible nitric oxide synthase and beta-catenin pathways in colon cancer cells. *Carcinogenesis*, 2004. **25**(12): p. 2443-9.
153. Nano, J.L., et al., Effects of Fatty Acids on the Growth of Caco-2 Cells. *Prostaglandins Leukotrienes and Essential Fatty Acids*, 2003. **69**: p. 207-215.
154. Reddy, B.S., *Carcinogen-induced colon cancer models for chemoprevention and nutritional studies.*, in *Tumour models in cancer research*, B.A. Teicher, Editor. 2002, Totowa, N.J: Humana Press. p. 183-191.
155. Reddy, B.S., Studies with the azoxymethane-rat preclinical model for assessing colon tumor development and chemoprevention. *Environ Mol Mutagen*, 2004. **44**(1): p. 26-35.
156. Kawamori, T., et al., Chemopreventative effect of curcumin, a naturally occurring antiinflammatory agent, during the promotion/progression stages of colorectal cancer. *cancer research*, 1998. **59**: p. 597-601.
157. Sohn, O.S., et al., Metabolism of azoxymethane, methylaoxymethanol and N-nitrosodimethylamine by cytochrome P4502E1. *Carcinogenesis (Lond)*, 1991. **12**: p. 127-131.
158. Fiala, E.S., Investigations into the metabolism and mode of action of the colon carcinogens 1,2-dimethylhydrazine and azoxymethane. *Cancer*, 1977. **40**(5 Suppl): p. 2436-45.

159. Shamsuddin, A., Comparative studies of primary, metastatic and transplanted adenocarcinomas of Fischer 344 rats. *J. Submicrosc Cytol*, 1994. **16**: p. 697-704.
160. Elwell, M.R. and E.S. McConnell, *Small and large intestine.*, in *Pathology of the Fischer rat.*, G.A. Boorman, et al., Editors. 1990, Academic Press: San Diego, CA. p. 43-61.
161. Takahashi, M. and K. Wakabayashi, Gene mutations and altered gene expression in azoxymethane-induced colon carcinogenesis in rodents. *Cancer Sci*, 2004. **95**(6): p. 475-80.
162. Singh, J., et al., Modulation of azoxymethane-induced mutational activation of ras protooncogenes by chemopreventative agents in colon carcinogenesis. *Carcinogenesis*, 1994. **15**: p. 1317-1323.
163. Takahashi, M., et al., Beta-Catenin is frequently mutated and demonstrates altered cellular location in azoxymethane-induced rat colon tumours. *Cancer Research*, 1998. **58**: p. 42-46.
164. Corpet, D.E. and F. Pierre, Point: from animal models to prevention of colon cancer. Systematic review of chemoprevention in min mice and choice of the model system. *Cancer Epidemiol Biomarkers Prev* 2003. **12**(5): p. 391-400.
165. Reeves, P.G., F.H. Nielsen, and G.C. Fahey, AIN-93 purified diets for laboratory rodents: final report of the American Institute of Nutrition ad hoc writing committee on the reformulation of the AIN-76A rodent diet. *Journal of Nutrition*, 1993. **123**: p. 1939-1951.
166. Birkett, A.M., et al., Dietary intake and faecal excretion of carbohydrate by Australians: importance of achieving stool weights greater than 150g to improve faecal markers relevant to colon cancer risk. *Eur J Clin. Nutr.*, 1997. **51**(625-632).
167. Patten, G.S., et al., Dietary fish oil alters the sensitivity of Guinea pig ileum to electrically driven contractions and 8-iso-PGE₂. *Nutrition Research*, 2002. **22**(1413-1426).
168. Cardini, G., A. Giannini, and L. Lancioni, Characterisation of aberrant crypt foci in carcinogen-treated rats: association with intestinal carcinogenesis. *Br J Cancer*, 1995. **71**(4): p. 763-9.

169. Phillips, D.H., A. Hewer, and V.M. Arlt, 32P-postlabeling analysis of DNA adducts. *Methods Mol Biol*, 2005. **291**: p. 3-12.
170. Poirier, M.C., R. Santella, and A. Weston, Carcinogen macromolecular adducts and their measurement. *Carcinogenesis*, 2000. **21**(3): p. 353-359.
171. Thomale, J., et al., *Monoclonal antibody-based quantification and repair analysis of specific alkylation products in DNA*, in *Technologies for detection of DNA damage and mutations.*, G.P. Pfeifer, Editor. 1996, Plenum Press: New York. p. 87-101.
172. Merritt, A.J., et al., Apoptosis in small intestinal epithelial from P53 null mice: Evidence for a delayed P53-independent G2/M associated cell death after gamma irradiation. *Oncogene*, 1997. **14**: p. 2759-2766.
173. Rijke, R.P.C., H.M. Plaisier, and N.J. Langendoen, Epithelial cell kinetics in the descending colon of the rat. *Virhows Arch. B Cell Path.*, 1979. **30**: p. 85-94.
174. Potten, C.S., J.W. Wilson, and C. Booth, Regulation and significance of apoptosis in the stem cells of the gastrointestinal epithelium. *Stem Cells*, 1997. **15**(2): p. 82-93.
175. Li, Y.Q., et al., Target cells for the cytotoxic effects of carcinogens in the murine small bowel. *Carcinogenesis*, 1992. **13**: p. 361-368.
176. Willingham, M.C., Cytochemical methods for the detection of apoptosis. *J. Histochem and Cytochem*, 1999. **47**: p. 1101-1109.
177. Hughes, R. and I.R. Rowland, Stimulation of apoptosis by two prebiotic chicory fructans in the rat colon. *Carcinogenesis*, 2001. **22**(43-47).
178. Bromley, M., et al., A comparison of proliferation markers (BrdUrd, Ki-67, PCNA) determined at each cell position in the crypts of normal human colonic mucosa. *European Journal of Histochemistry*, 1996. **40**: p. 89-100.
179. Zedek, M.S., D.J. Grab, and S.S. Sternberg, Differences in the acute response of the various segments of rat intestine to treatment with the intestinal carcinogen, methyl azoxymethanol acetate. *Cancer research*, 1977. **37**: p. 32-36.
180. Sunter, J.D., D.R. Appelton, and A.J. Watson, Acute changes occurring in the intestinal mucosa of rats given a single injection of 1,2-dimethylhydrazine. *Cell pathology*, 1981. **36**: p. 47-57.

181. Kaina, B., et al., MGMT: Key node in the battle against genotoxicity, carcinogenicity and apoptosis induced by alkylating agents. *DNA Repair*, 2007. **6**: p. 1079-1099.
182. Liu, L., Y. Nakatsuru, and S.L. Gerson, Base excision repair as a therapeutic target in colon cancer. *Clinical Cancer Research*, 2002. **8**: p. 2985-2991.
183. Stivers, J.T. and Y.L. Jiang, A mechanistic perspective on the chemistry of DNA repair glycosylases. *Chem. Rev.*, 2003. **103**: p. 2729 - 2759.
184. Dizdaroglu, M., Base-excision repair of oxidative DNA damage by DNA glycosylases. *Mutation Research*, 2005. **591**: p. 45-59.
185. Wilson, D.M. and D. Barsky, The major human abasic endonuclease: formation, consequences and repair of abasic lesions in DNA. *Mutation Research*, 2001. **485**: p. 283-307.
186. Liuzzi, M. and M. Talpeart-Borle, A new approach to the study of the base-excision repair pathway using methoxyamine. *J Biol Chem*, 1985. **260**: p. 5252-5258.
187. Rosa, S., et al., Processing *in vitro* of an abasic site reacted with methoxyamine: a new assay for the detection of abasic sites formed *in vivo*. *Nucleic Acids Res*, 1991. **19**: p. 5569-5574.
188. Horton, J.K. and S.H. Wilson, Hypersensitivity phenotypes associated with genetic and synthetic inhibitor-induced base excision repair deficiency. *DNA repair*, 2007. **6**: p. 530-543.
189. Liu, L., et al., Pharmacological disruption of base excision repair sensitises mismatch repair deficient and proficient colon cancer cells to methylating agents. *Clin Cancer Res*, 1999. **5**(2908-2917).
190. Hoffmann, G.R., Genetic effects of dimethyl sulfate, diethyl sulfate and related compounds. *Mutation Research*, 1980. **75**: p. 63-129.
191. Ezaz-Nikpay, K. and G.L. Verdine, The effects of N-7-methyl-guanine on duplex DNA structure. *Chem Biol*, 1994. **1**: p. 235-240.
192. Engelward, B.P., et al., A chemical and genetic approach together define the biological consequences of 3-methyl-adenine lesions in the mammalian genome. *J. Biol. Chem.*, 1998. **273**: p. 5412-5418.

193. Smith, S.A. and B.P. Engelward, In vivo repair of methylation damage in Aag 3-methyladenine-DNA glycosylase null mouse cells. *Nucleic Acids Res*, 2000. **28**: p. 3294-3300.
194. Singh, J., R. Hamid, and B.S. Reddy, Dietary fat and colon cancer: modulation of cyclooxygenase-2 by types and amount of dietary fat during the postinitiation stage of colon carcinogenesis. *Cancer Res*, 1997. **57**(16): p. 3465-70.
195. Le Leu, R., Y. Hu, and G.P. Young, Effects of resistant starch and nonstarch polysaccharides on colonic luminal environment and genotoxin-induced apoptosis in the rat. *Carcinogenesis*, 2002. **23**(713-719).
196. Roediger, W.E., Utilization of nutrients by isolated epithelial cells of the rat colon. *Gastroenterology*, 1982. **83**: p. 424-429.
197. Geypens, B., et al., Influence of dietary protein supplements on the formation of bacterial metabolites in the colon. *Gut*, 1997. **41**(70-76).
198. Wogan, G.N., et al., Environmental and chemical carcinogenesis. *Semin Cancer Biol*, 2004. **14**(6): p. 473-86.
199. Yao, H.T., et al., The inhibitory effect of polyunsaturated fatty acids on human CYP enzymes. *Life Sciences*, 2006. **79**(26): p. 2432-40.
200. Sohn, O.S., et al., Differential effects of CYP2E1 status on the metabolic activation of the colon carcinogens aoxymethane and methylazoxymethanol. *Cancer Research*, 2001. **61**(23): p. 8435-40.
201. Brady, J.F., et al., Effects of disulfiram on hepatic P4502E, other microsomal enzymes and hepatotoxicity in rats *Toxicol Appl Pharmacol*, 1991. **108**(2): p. 366-73.
202. Ding, X. and L.S. Kaminsky, Human extrahepatic cytochromes P450: Function in xenobiotic metabolism and tissue-selective chemical toxicity in the respiratory and gastrointestinal tracts. *Annu Rev Pharmacol. Toxicol.*, 2003. **43**: p. 149-73.
203. Cohen, P.A., et al., Immunohistochemical determination of hepatic cytochrome P-4502E1 in formalin fixed paraffin embedded sections. *Alcohol Clin Exp Res*, 1997. **21**(6): p. 1057-62.
204. Bruce, W.R., et al., Diet, Aberrant crypt foci and colorectal cancer. *Mutation research*, 1993. **290**(1): p. 111-118.

205. Zheng, Y., et al., Effect of retinoids on AOM-induced colon cancer in rats: modulation of cell proliferation, apoptosis and aberrant crypt foci. *Carcinogenesis*, 1999. **20**(2): p. 255-60.
206. Pretlow, T.P., M.A. O'Riordan, and G.A. Somich, Aberrant crypts correlate with tumor incidence in F344 rats treated with azoxymethane and phytate. *Carcinogenesis*, 1992. **13**(9): p. 1509-12.
207. Wijnands, M.V., et al., Do aberrant crypt foci have predictive value for the occurrence of colorectal tumours? Potential of gene expression profiling in tumours. *Food Chem Toxicol*, 2004. **Oct 42**(10): p. 1629-39.
208. Park, H.S., R.A. Goodlad, and N.A. Wright, The incidence of aberrant crypt foci and colonic carcinoma in dimethylhydrazine-treated rats varies in a site-specific manner and depends on tumor histology. *Cancer Research*, 1997. **57**(20): p. 4507-10.
209. Magnuson, B.A. and R.P. Bird, Ability of aberrant crypt foci characteristics to predict tumour incidence in rats fed cholic acid. *Cancer research*, 1993. **53**(19): p. 4499-504.
210. Bird, A.R., Observation and quantification of aberrant crypts in the murine colon treated with a colon carcinogen: preliminary findings. *Cancer letters*, 1987. **37**: p. 147-151.
211. GP, Y., et al., Wheat bran suppresses potato starch-potentiated colorectal tumorigenesis at the aberrant crypt stage in a rat model. *Gastroenterology*, 1996. **110**: p. 108-14.
212. McIntyre, A., et al., Different fibers have different regional effects on luminal contents of rat colon. *Gastroenterology*, 1991. **101**: p. 1274-1281.
213. Kaina, B., Mechanisms and consequences of methylating agent-induced SCEs and chromosomal aberrations: a long road traveled and still a far way to go. *Cytogenet Genome Res*, 2004. **104**(1-4): p. 77-86.
214. Duckett, D.R., et al., Human MutS α recognizes damaged DNA base pairs containing O6-methylguanine, O4-methylthymine, or the cisplatin-d(GpG) adduct. *Proc Natl Acad Sci U S A*, 1996. **93**(13): p. 6443-7.
215. Karran, P., Mechanisms of tolerance to DNA damaging therapeutic drugs. *Carcinogenesis*, 2001. **22**: p. 1931-7.

216. Young, G.P., et al., Wheat bran suppresses potatoe starch potentiated colorectal tumourigenesis at the aberrant crypt stage in a rat model. *Gastroenterology*, 1996. **110**(2): p. 508-14.