

## Subject Index

- Aberrant crypt foci, 7, 103, 116  
Acetaldehyde, 216, 247, 248, 249, 279  
*N*-Acetylcysteine, 261  
*N*-Acetyltransferase, 5, 36, 142, 181, 182, 243, 276  
Actinic keratoses, 7, 85, 88  
Adducts, *see* DNA adducts, Protein adducts  
Adenoma  
  colorectal, 7, 14, 15, 18, 21, 103, 105, 113–116, 133  
  hepatic, 223, 226  
Adenomatous atypical hyperplasia, 192, 200, 265  
Aerodigestive tract, 5, 18, 34, 37, 257, 261, 272  
Aflatoxins, 5  
  albumin adducts, 41, 216, 217  
  DNA adducts, 32, 216, 218, 242  
  and liver cancer, 216, 218–220, 223, 241  
  metabolites, 31, 216  
  protein adducts, 31, 217  
Age, 119, 131, 132, 166  
Ageing, breast tissue, 163, 166  
AIDS, 21, 38, 39  
Albinism, 93  
Albumin adducts, 31, 41, 216–218, 249  
Alcohol  
  and colorectal cancer, 62, 65  
  and liver cancer, 5, 216, 223, 241  
  metabolism, 279  
  and oral cancer, 247, 271  
2-Amino-1-methyl-6-phenylimidazo[4,5-*b*]-pyridine, *see* PhIP  
Δ4-Androstenedione, 150, 151  
Androgens, 5, 150, 157, 193, 199, 201–203, 208  
Angiogenesis, 194  
Antiestrogens, 16  
Antioxidants, 4, 58, 97, 105, 191, 208, 232  
α-1-Antitrypsin deficiency, 241  
APC gene, 15, 20, 22, 33, 37, 115, 117, 134–140  
Apoptosis, 15, 154, 192, 194, 258  
Aromatase, 151, 157, 180  
Ashkenazi Jews, 140, 144, 179  
Aspirin, 37  
Ascorbic acid, *see* Vitamin C  
Ataxia telangiectasia, 37, 180  
Barrett's oesophagus, 8, 14, 20  
Benzo[a]pyrene, 245, 247, 272  
Betel quid, 247, 249, 272  
Bias, 63–65  
Biomarkers, 27  
  definition, 1  
  exposure, 3–6, 29–32  
  intermediate effect, 6–8, 13–22  
  predictive value, 50  
  prognostic value, 38  
  surrogacy, 38–41  
  susceptibility, 8–10  
  validity, 2, 5, 29, 57, 63, 70  
Bile acids, 102, 105  
Bladder, urinary  
  cancer, 18, 20, 34, 36, 58  
  precancer, 14  
Bloom's syndrome, 37  
Bowel, large, *see* Colorectum  
Bowman–Birk inhibitor, 53  
Bran, 119  
Breast  
  *ATM* gene, 180  
  *BRCA* genes, 15, 37, 62, 178–184  
  cancer, 34, 37  
    and diet, 149  
    and hormonal factors, 5, 149–159, 163, 166, 180  
  density, 7, 163–167, 173  
  ductal carcinoma *in situ*, 7, 14, 35, 171–174  
  intermediate-effect biomarkers, 163–167, 171–174  
  mammography, 7, 163, 173, 174  
  screening, 173, 174, 182  
  susceptibility biomarkers, 177–184  
  tamoxifen trial, 49, 184  
Broccoli, 38, 281  
Calcium, 101, 105, 115, 116  
Calprotectin, 104  
Carbohydrates, 149  
Carcinoembryonic antigen, 32, 117  
Carcinoid tumours, 32  
β-Carotene, 5, 58, 105, 116, 119, 141, 259–262, 279, 280  
Carotenoids, 9  
Catechins, 280  
Catechol-O-methyltransferase (COMT), 152–154, 180, 182  
β-Catenin, 115, 137  
CD44, 118  
Celecoxib, 21, 22, 37  
Cervix uteri, cancer of, 3, 32, 38  
Children, 87, 139  
Chlorophyllin, 220  
Chromosome alterations, 18, 172–173  
Cigarette smoking, *see* Tobacco  
Cirrhosis, 241  
Clofibrate, 232  
Colorectum  
  aberrant crypt foci, 7, 103, 116  
  adenomas, 7, 14, 15, 18, 21  
  cancer, 20, 21, 36, 37, 62, 101  
    and alcohol, 65  
    dietary factors, 101, 105–108, 115  
  DNA adducts, 104  
  exposure biomarkers, 5, 101–104  
  intermediate-effect biomarkers, 7, 103, 113–120  
  intervention trials, 52, 105–108  
  *p53* mutations, 117  
  susceptibility biomarkers, 131–144  
  *see also* Hereditary non-polyposis colorectal cancer and Familial adenomatous polyposis  
Confounding, 65  
Contraceptives, oral, 156, 241  
Cotinine, 5  
Cowden syndrome, 178  
COX-2, 5, 10, 16, 62  
Cyclins, 18, 172  
Cyclobutane pyrimidine dimers, 69  
Cytochrome P450 (CYP), 5, 97, 152, 180, 242, 272–275, 277–278, 281  
  CYP1A1, 97, 242, 250, 272  
  CYP1A2, 65, 219, 250, 277, 281  
  CYP2A6, 242, 277  
  CYP1B1, 277  
  CYP2B6, 242  
  CYP2C9, 277  
  CYP2C19, 277  
  CYP2D6, 97, 250, 274  
  CYP2E1, 65, 250, 274  
  CYP3A2, 208  
  CYP3A4, 210, 217, 277  
  CYP17, 208  
  CYP19, 182  
Dehydroepiandrosterone, 151, 157, 228, 231–234  
Detoxification, 58, 96, 142, 154, 216, 245, 249, 272, 276, 281  
Diabetes, 229  
Dietary factors, 58  
  breast cancer, 149  
  colorectal cancer, 101, 105–108, 115

- liver cancer, 216, 241  
prostate cancer, 191
- 2-Difluoromethylomithine, 18, 22, 37, 51–53
- DNA adducts, 5, 6, 8, 29, 31, 57–58, 104, 271  
aflatoxin, 32, 216, 218, 242  
bulky, 58, 273, 277, 278  
etheno, 5, 104, 108  
exocyclic, 272  
postlabelling analysis, 31, 58, 104, 247  
in skin, 4  
tobacco carcinogens, 245, 247, 273  
methylation, 34, 248, 264  
repair, 8, 36, 58, 61, 70, 74, 94, 103, 133, 138, 181  
synthesis, unscheduled, 8
- Ductal carcinoma *in situ*, 7, 14, 35, 171–174
- Dysplasia, 8, 113, 258, 265
- Endocrine factors, *see* Hormones
- Enzyme antioxidant, 97  
carcinogen-metabolizing, 9, 35, 58, 241, 271–282  
DNA repair, 35, 37, 58, 74  
induction, 272, 280, 281, 282  
steroid-metabolizing, 151–154  
*see also* Cytochrome P450,  
Glutathione S-transferase
- Epidermal growth factor (EGF), 16, 18
- Estradiol, 150, 151, 158
- Estrogens, 150–156, 166
- Estrogen receptor, 16, 18
- Ethanol, *see* Alcohol
- Etheno adducts, 5, 104, 108
- Ethical issues, 10, 143
- Exercise, 115, 149, 157
- Exposure biomarkers, 3, 29–32  
breast, 149–159  
colon, 5, 101–104  
liver, 3, 215–220  
lung, 245–251  
prostate, 191  
skin, 4, 69–78  
validation, 5
- Faecal occult blood test, 101, 104
- Familial adenomatous polyposis, 9, 18, 20, 37, 103, 104, 116, 119, 131, 136–138, 142
- Fanconi's anaemia, 37
- Fat, 101, 115, 116, 119, 149, 191
- Fenretinide, 156, 184, 259
- $\alpha$ -Fetoprotein, 32
- Fibre, 101, 105, 115, 116
- Field cancerization, 257
- Finasteride, 202, 211
- Fish oil, 119
- Flavonoids, 158
- Fluorescent bronchoscopy, 265
- Foci of altered hepatocytes, 223–229, 233–235
- Folate, 115, 141
- Food, *see* Dietary factors
- Fruit, 58, 61, 107, 115, 116
- Gene amplification, 16  
*APC*, 15, 20, 22, 33, 37, 115, 134–140  
*AR*, 209  
*ATM*, 180  
*BRCA*, 15, 37, 62, 178–184  
*CDKN2A*, 95  
*COMT*, 154, 180, 182  
DNA repair, 35, 37, 94, 133, 138  
*HPRT*, 33  
*MOM1*, 131, 140  
*MSH2*, 140, 178  
*MTHFR*, 141  
*NAT2*, 5, 36, 142, 181, 182, 243, 276  
penetrance, 8, 10, 35, 62  
*PTCH*, 95  
*PTEN*, 139, 178  
*ras*, 15, 33, 95, 115, 117, 135, 263, 265  
*SHH*, 95  
*SMO*, 95  
*SRDA5A2*, 209, 211  
*see also* Cytochrome P450,  
Glutathione S-transferase and p53
- Genetic polymorphism, *see* Polymorphism
- Genomic instability, 32, 34, 263
- Glucose-6-phosphate dehydrogenase, 233
- Glucuronides, 30, 153
- $\gamma$ -Glutamyltranspeptidase, 228, 233
- Glutathione S-transferase (GST), 38, 218, 272, 281  
*GSTM1*, 5, 36, 63, 96, 97, 181–183, 242, 273, 275, 280, 282  
*GSTM3*, 275, 276  
*GSTP1*, 96, 181–183, 228, 275, 276, 282
- GSTT1, 96, 181, 275, 276, 282  
and breast cancer, 181–183  
and liver cancer, 233  
and lung cancer, 275–276  
and skin cancer, 96, 97
- Glycogen, 226–230
- Glycophorin A assay, 33
- Gorlin's syndrome, 139
- Growth hormone-releasing hormone, 155
- Haemochromatosis, 241
- Haemoglobin adducts, 31, 249
- Head and neck cancer, 16, 18, 261  
(*see also* Oral cancer)
- Hepatitis viruses, 3  
and liver cancer, 5, 33, 215, 220, 223, 241
- vaccination, 218
- Hepatocellular carcinoma (HCC), *see* Liver, cancer of
- Hereditary non-polyposis colorectal cancer, 9, 16, 37, 119, 131–133, 138–139, 178
- Heterocyclic amines, 5, 30, 32, 36, 65, 104, 141, 277
- Heterogeneous nuclear ribonucleoprotein (hnRNP), 7, 262
- Homocysteine, 62
- Hormones  
and breast cancer, 5, 149–159, 163, 166, 180  
exogenous, 149  
insulin, 151, 154–158, 229  
and liver cancer, 229, 232  
and prostate cancer, 5, 201–203  
replacement therapy, 156, 159, 166  
steroids, 150–154, 157, 180  
thyroid, 232, 234
- Human immunodeficiency virus, 38, 39
- Human papillomavirus, 3, 38
- 5-Hydroxyindoleacetic acid, 32
- 8-Hydroxydeoxyguanosine, 5, 61
- Iceland, 179
- Immunosuppression, 85
- Inflammatory bowel disease, 134
- Insulin, 151, 155, 156, 158, 229
- Insulin-like growth factors, 16, 150, 154–159, 208, 231
- Intermediate effect biomarkers, 6–8, 13–22, 32–35, 49  
breast, 163–167, 171–174  
colon, 7, 103, 113–120  
liver, 223–235

- lung, 257–266  
prostate, 191–197, 200–203  
skin, 81–89
- Intervention studies, 16, 27  
breast, 34, 155–158, 184  
colorectum, 52, 105–108, 116  
liver, 7, 218, 220  
lung, 259–262, 266, 279  
oltipraz, 31, 38  
population selection, 3, 8, 9, 18, 27, 35, 283  
phase I, 19  
oral leukoplakia, 53  
phase II, 2, 18  
breast, 7, 19  
colon, 52  
liver, 220  
oral leukoplakia, 53  
prostate, 19  
phase III, 2, 18  
breast, 157  
colon, 53  
prostate, 19, 210–211
- Intraepithelial neoplasia, 8, 13, 15, 35  
cervical, 35  
ductal carcinoma *in situ*, 7, 14, 35  
prostate, 7, 14, 35, 191–197, 200–203
- 8-Isoprostanate F-2 $\alpha$ , 61  
Isothiocyanates, 5, 31, 38, 248, 250, 281  
Isotretinoin, 259
- Juvenile polyposis, 139
- Kidney tumours, 34  
Knock-out mice, 10
- Labelling index, 118, 119  
Large bowel, *see* Colorectum  
Leukaemia, 37  
Leukoplakia, 53  
Li-Fraumeni syndrome, 10, 37, 95, 178  
Linoleic acid, 108  
Lipid peroxidation, 5, 104, 108, 272, 279  
Liver  
angiosarcoma, 215  
cancer of, 32, 215  
and aflatoxins, 5, 7, 33, 218, 223  
and alcohol, 5, 223  
and hepatitis viruses, 5, 33, 215, 220, 223, 241  
*p53* mutations, 7, 38, 218  
hepatocellular carcinoma, 7, 41, 215, 220
- 223, 241  
intermediate effect biomarkers, 223–235  
susceptibility biomarkers, 241–243
- Lobular carcinoma *in situ*, 35, 171  
Loss of heterozygosity, 16, 258, 263  
Lung, cancer of, 34, 37  
atypical cells in sputum, 7, 259, 261  
and GST polymorphism, 63  
exposure biomarkers, 245–251  
intermediate effect biomarkers, 257–266  
non-small-cell, 34  
and oxidative stress, 272  
*p53* mutations, 263  
retinoic acid receptor  $\beta$ , 7, 258  
second primary, 261, 262  
and smoking, 245, 257  
susceptibility biomarkers, 271–283
- Luteinizing hormone, 157  
Lycopene, 191, 208  
Lymphoma, 37  
Lynch syndrome, *see* Hereditary non-polyposis colorectal cancer
- Mammography, 7, 163, 173, 174, 184  
Measurement error, 57, 61, 113, 117  
Meat, 58, 101, 104, 115, 119, 141  
Melanin, 94  
Melanoma, 7, 70, 81, 86–87, 93 (*see also* Skin, cancer)  
Menopause, 166  
Mercapturic acids, 30  
Metabolism, 9  
of chemopreventive agents, 38  
carcinogen, 35, 219, 271–282  
oxidative, 35  
steroid hormone, 151, 153, 155, 180
- Metabolites  
carcinogenic, 61  
urinary, 30–31, 216, 249
- Metaplasia, bronchial, 258, 261  
Methionine, 62  
Methylation, DNA, 34, 248, 264  
Methylenetetrahydrofolate reductase, 62, 141  
4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), 30, 245, 272, 274, 277, 282
- Microsatellites, 16, 34, 134, 138, 210, 263  
Mismatch repair, 37, 133, 134, 138  
Monooxygenase, *see* Cytochrome P450  
Muir–Torre syndrome, 178  
Mutations, 8, 32, 271  
*ATM* gene, 180
- APC* gene, 9, 22, 37, 115, 117, 135–140  
breast cancer genes, 37, 178  
 $\beta$ -catenin, 115  
mismatch repair genes, 37, 138  
*MSH2*, 178  
*p53* gene, 10, 37  
in colorectal cancer, 115, 116, 117  
in liver cancer, 7, 33, 218, 220, 242  
in lung tumours, 263, 274  
in skin tumours, 7, 82  
*PTEN* gene, 139, 178  
*ras* gene, 115, 117, 135, 263  
screening, 179, 182  
*STK11*, 178  
tyrosinase gene, 94
- NAD(P)H:quinone oxidoreductase (NQO1), 97, 278  
Naevus, 4, 7, 84, 87, 89, 95, 139  
*NAT2* gene, 36, 142, 181, 182, 243, 276  
Nicotine, 31, 245, 251, 274, 277  
Nitrosamines, 32, 245, 247–250, 277  
*N*-Nitrosornornicotine, 272, 274, 278  
Nonsteroidal anti-inflammatory drugs, 9, 18, 21, 22, 119  
Nutrition, *see* Dietary factors
- Obesity, 115, 149, 151, 155, 157, 191  
Oesophagus, Barrett's, 8, 14, 20  
Ooltipraz, 31, 38, 41, 218, 232  
Oncogene, 14, 18 (*see also* specific genes)
- Oral cancer  
leukoplakia, 53, 276  
susceptibility markers, 271–283  
and tobacco use, 247, 271
- Ornithine decarboxylase, 18, 51
- Ovary, cancer of, 178
- Overtreatment, 174
- Oxidative stress, 4, 5, 6, 8, 97, 272
- 8-Oxodeoxyguanosine, 32, 104, 248
- p53*, 18  
and breast cancer, 18  
gene mutations, 7, 10  
in colorectal cancer, 117  
Li-Fraumeni syndrome, 10, 37, 178  
in liver cancer, 7, 33, 218, 220, 242  
in lung tumours, 263, 274  
in skin tumours, 7, 82
- knock-out mice, 10

- polymorphism, 242, 243  
 Papanicolaou test, 32  
 Parity, 165  
 Penetrance, gene, 8, 10, 35, 62  
 Peroxisome proliferators, 231–234  
 Peutz–Jeghers syndrome, 139, 178  
 Phenobarbital, 32  
 Phenyl isothiocyanate, 31, 248, 250, 281  
 PhIP, 104  
 Photoproducts, 32, 69  
 Physical activity, *see* Exercise  
 Phytoestrogens, 158  
 Polycyclic aromatic hydrocarbons, 5, 32, 245, 247, 249, 272, 273  
 Polycystic ovary syndrome, 150, 157  
 Polymorphism, genetic, 8, 36, 271–283  
   *N*-acetyltransferase, 5, 36, 142, 276  
   APC, 139  
   CYP genes, 97, 242, 272–274, 277–278  
   COMT, 154  
   glutathione S-transferase (GST), 36, 38, 96, 275–276  
   methylenetetrahydrofolate reductase, 62, 141  
   *p53*, 242, 243  
   SRDA5A2, 209, 211  
   VDR, 210  
   xenobiotic-metabolism, 36, 217, 271–282  
 Polyps, *see* Adenoma  
 Polyphenols, 5, 280, 282  
 Postlabelling, 31, 58, 69–71, 104, 247  
 Predictive value of biomarker, 50  
 Progesterone, 150, 166  
 Progestogens, 150  
 Prognostic value of biomarker, 38  
 Prolactin, 167  
 Proliferating cell nuclear antigen, 118  
 Proliferation, 15, 16, 103, 105, 116, 135, 154, 192, 224, 232  
   mucosal, 118–120, 194  
 Proportionate risk, 50  
 Prostate  
   cancer, 191, 199  
   exposure biomarkers, 5  
   hormonal effects, 5, 201–203  
   intraepithelial neoplasia, 7, 14, 191–197, 200–203  
   -specific antigen, 18, 32, 194, 200, 203  
   susceptibility biomarkers, 207–211  
 Protein adducts, 29, 31, 249  
 Quality of life, 20  
 Radiation, 224, 226  
 Raloxifene, 156, 184  
*ras* gene, 15, 33, 95, 115, 117, 135, 263, 265  
 Reactive oxygen species, 94, 96, 97, 272, 278  
 Recommendations, 11  
 Renal cancer, 34  
 Replacement therapy, 156, 159, 166  
 Retinoblastoma, 37, 95  
 13-*cis*-Retinoic acid, 258, 261  
 all-*trans*-Retinoic acid, 279  
 Retinoids, 184, 258, 259, 279  
 Retinyl palmitate, 261, 279  
 Screening  
   for breast cancer, 173, 174, 182  
   familial adenomatous polyposis, 142  
   mutation, 179  
   for prostate cancer, 199, 201, 203  
 Second primary lung cancer, 261, 262  
 Selenium, 5, 105, 194, 208, 261  
 Sex hormone binding globulin, 150, 151, 155, 157, 158, 208  
 Skin  
   cancer, 36, 37, 69, 81–82, 93–98  
     (*see also* Melanoma)  
   colour, 76  
   exposure biomarkers, 4, 69–78  
   intermediate-effect biomarkers, 7  
   *p53* mutations, 7, 82  
   susceptibility biomarkers, 93–98  
 Smoking, *see* Tobacco  
 Solar radiation, 69, 81  
 Somatostatin, 155  
 Soybean, 53  
 Sputum atypia, 7, 259, 261  
 Steroids, 150–154, 157, 180  
 Sulfate esters, 30, 153  
 Sulindac, 22, 37, 53, 116, 119  
 Sunburn, 7, 69, 82, 88, 93  
 Sunscreen, 75, 82, 85, 93, 97  
 Surrogacy, 38–41  
 Surrogate end-point biomarkers, 13–22, 29 (*see also* Intermediate-effect biomarkers)  
 Susceptibility biomarkers, 8–10, 35–38  
   breast cancer, 177–184  
   colorectal cancer, 131–144  
   liver cancer, 241–243  
   lung, 271–283  
   prostate cancer, 207–211  
   skin cancer, 93–98  
 Tamoxifen, 49, 62, 156, 159, 174, 184  
 Tanning, 70, 75  
 Tea, 234, 280  
 Testosterone, 150, 157, 201  
 Thymidine glycol, 32  
 Thyroid, 32, 232, 234  
 Tobacco smoking  
   carcinogen metabolism polymorphism, 271–283  
   carcinogens, 246, 272  
   chewing, 272  
   and lung cancer, 245, 257, 271, 274  
   and oral cancer, 271  
   and oxidative stress, 272  
   -specific nitrosamines, 32, 245, 247–250, 272, 277  
 Tocopherols, 5, 262 (*see also* Vitamin E)  
 Transforming growth factor (TGF), 16, 18, 115, 134, 138  
 Transgenic mice, 6, 8, 9, 226, 242  
 Trials, *see* Intervention studies  
 Tumour-suppressor genes, 15, 18, 37, 179, 263 (*see also* specific genes)  
 Turcot's syndrome, 139  
 Tyrosinase, 94  
 Ulcerative colitis, 134  
 Ultraviolet radiation, 36, 69, 81, 93  
*cis*-Urocanic acid, 86  
 Vaccination, 218, 223  
 Validity, 2, 5, 29, 63  
 Vegetables, 9, 58, 61, 65, 107, 115, 116, 281, 282  
 Vinyl chloride, 215  
 Vitamins  
   A, 119, 258, 261, 279  
   C (ascorbic acid), 32, 105, 116, 119  
   D, 180, 208, 210  
   E ( $\alpha$ -tocopherol), 58, 105, 116, 119, 194, 208, 259, 261, 280  
 Watercress, 30, 250, 282  
 Wnt signalling, 137  
 Xenobiotic metabolism, 9, 35, 58  
 Xeroderma pigmentosum, 36, 37, 70, 94