Foreword

This special supplement to the *Journal of Cellular Biochemistry* is the eleventh in a series produced by the National Cancer Institute (NCI), Division of Cancer Prevention and Control, Chemoprevention Branch. Nine of the previous supplements contain the proceedings of conferences sponsored by the Chemoprevention Branch. The tenth (Supplement 20) was published in conjunction with one of the conferences, *Cancer Chemopreventive Agents: Drug Development Status and Future Prospects*, held in Princeton, New Jersey in October 1994.

The manuscripts in that supplement provide an overview of NCI, Chemoprevention Branch drug development strategies including chemopreventive mechanisms as a basis for drug discovery, NCI/FDA consensus guidance for evaluation of chemopreventive drugs, and preclinical efficacy studies in animal cancer models. The remainder and majority of the volume are Clinical Development Plans for 16 promising chemopreventive agents, most of which are well into clinical studies: *N*-acetyl-*l*-cysteine (NAC), aspirin, calcium, β-carotene, dehydroepiandrosterone (DHEA) analog 8354 (fluasterone), 2-difluoromethylornithine (DFMO), finasteride (Proscar®), glycyrrhetinic acid, all-*trans*-*N*-(4-hydroxyphenyl)-retinamide (4-HPR), ibuprofen, oltipraz, piroxicam, sulindac, tamoxifen, vitamin D_3 and analogs, and vitamin E. The plans summarize the status of the agents regarding evidence for safety and chemopreventive efficacy in preclinical and clinical studies. They also include strategies for further development of the drugs that consider pharmacodynamics, drug effect measurements, intermediate biomarkers (particularly, potential surrogate endpoints for cancer incidence), toxicity, supply and formulation, requirements for regulatory approval, and future clinical trials.

The current volume continues reviewing chemoprevention drug development strategies. The first article describes the rationale for and development status of newer chemopreventive agents, many not yet evaluated in the Chemoprevention Branch drug development program. The second article considers *in vitro* chemopreventive efficacy screens and presents a survey of results obtained with these assays in the Chemoprevention Branch program. As in Supplement 20, the remainder of the volume is 16 Clinical Development Plans: curcumin, DHEA, folic acid, genistein, indole-3-carbinol, perillyl alcohol, phenethyl isothiocyanate (PEITC), 9-*cis*-retinoic acid, 13-*cis*-retinoic acid, *l*-selenomethionine, 1,4-phenylenebis(methylene)selenocyanate (*p*-XSC), sulindac sulfone, tea, ursodiol, vitamin A, and (+)-vorozole. While these agents have high promise as chemopreventives, some also raise new issues related to chemopreventive drug development. For example, the plans presented in Supplement 20 are primarily on well-tested drugs and vitamins. In contrast, many agents discussed in the current volume are in the very early stages of clinical development; plans on such agents place greater emphasis on mechanism of action and preclinical efficacy and toxicity evaluation. A few are derivatives or analogs of well-established chemopreventive agents; these agents may prove to have more clinical benefit than their parents because of improved efficacy (9-*cis*-retinoic acid) or reduced toxicity (sulindac sulfone). Several agents covered in this volume are derived from dietary components (*e.g.*, curcumin, genistein, tea). Standardized formulations are a critical aspect of developing these dietary substances.

The number of cancer chemoprevention research and development efforts has increased rapidly during the past five years. This special series of *Journal of Cellular Biochemistry* supplements is dedicated to keeping abreast of and promoting advances in this new medical science. To this end, volumes specifically on chemopreventive drug development strategies will continue to be published on a regular basis, in addition to those containing the proceedings of chemoprevention conferences.