Genotoxicology of N-Nitroso Compounds

TOPICS IN CHEMICAL MUTAGENESIS

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Edited by T. K. Rao, W. Lijinsky, and J. L. Epler

Volume 2 Single-Cell Mutation Monitoring Systems: Methodologies and Applications

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Genotoxicology of N-Nitroso Compounds

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Foreword

Topics in Chemical Mutagenesis is a new series dedicated to studies in the areas of environmental chemical mutagenesis and genetic toxicology. In this series we will explore some of many topics that are emerging in these rapidly developing fields.

The purpose of the present volume is to attempt to organize and compare the genotoxic properties of the N-nitroso compounds. This is a particularly interesting class of compounds because of the problems encountered with the *Salmonella* assay of Ames in generating both false positive and false negative results. The battery approach using a number of assay systems seems more appropriate to evaluate chemicals in this class.

Topics to be discussed in other volumes in this series include single-cell mutation monitoring systems, the detection of genetic damage in mammalian germ cells, the mutagenicity of pesticides, problems in monitoring human populations in genetic toxicology, and a glossary of terms in genetic toxicology. All of these books are in various stages of development and should appear within the next few years.

Frederick J. de Serres
Series Editor

Preface

During the past ten years there has been an explosive development in the number of short-term tests to predict the biological risks, especially risks of cancer, in exposure to xenobiotic chemicals. The number of published articles in this area has reached many thousands a year and there are several new journals devoted almost entirely to the presentation of the results obtained in these tests. The developers and large-scale users of these tests often rival one another in their claims of validity as predictors of carcinogenicity. Many of the test systems have mutagenesis as the measured end point, and it is frequently forgotten that mutagenesis itself is a biological hazard and that the measurement of a mutagenic risk to man is of equal importance with the estimation of carcinogenic risk. A number of books and review articles have been written about the development and application of short-term assays for mutagenesis–carcinogenesis, but none has focused on the applications of these assays to a single group of well-tested carcinogens sufficiently large and important to be a guide to understanding the complex processes of mutagenesis and carcinogenesis and the relation between them.

Almost three years ago, Dr. F. J. de Serres organized a meeting at the National Institutes of Health that was attended by a number of scientists who had worked, sometimes cooperatively, sometimes alone, in examining the behavior of a single group of compounds, the N-nitroso compounds, in the assay with which they were most familiar. From this group of scientists, all of whom presented interesting data, several volunteered to pool their results in the compilation of a single volume that would be devoted to the comparison of the results obtained with N-nitroso compounds from mainly a single source of consistent chemical quality, and an evaluation of those results as a predictor of one assay system by another, and that would be a means of illuminating the complexity of the mechanisms of biological action of these toxicants. It is this

volume that we present as an effort to understand the meaning of all of the results, often disparate, that appear in the literature describing the application of all of these assay systems. The conclusions represent a consensus view of these combined efforts and are a beginning for the continuing process of unraveling the mechanisms of genetic toxicology through comparative studies of biological assays, based on a firm foundation of chemical structural relations among N-nitroso compounds.

T. K. Rao
W. Lijinsky
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