

Molecular mechanisms of metal toxicity and carcinogenesis

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Abstract

Many metals and metal-containing compounds have been identified to be potent mutagens and carcinogens. Recently, a new sub-discipline of molecular toxicology and carcinogenesis has been developed. The combination of newly developed molecular techniques and free radical approach makes it possible to insightfully examine metal-induced carcinogenesis in precise molecular terms so that intricate biological interrelationships can be elucidated. In consideration of the increased amount of new findings deciphered by utilizing these new methods, the 1st Conference on Molecular Mechanisms of Metal Toxicity and Carcinogenesis was held. In this conference, more than 50 scientists from nine countries presented their novel discoveries concerning metal-induced carcinogenesis, delineated molecular mechanism of metal carcinogenesis, and proposed novel therapeutic intervention and prevention strategies. This article reviews some of the state-of-the-art information presented at the meeting regarding the molecular mechanisms of metal cytotoxicity and carcinogenesis. (*Mol Cell Biochem* 222: 3–9, 2001)

Key words: ROS, cell growth regulation, transcription factor, signal transduction, cytotoxicity and carcinogenesis

Introduction

Both environmental and occupational exposures to chromium (Cr), nickel (Ni), and arsenic (As) compounds have been reported to cause human tumors in various systems [1, 2]. Although a variety of metals, including Cr, Ni, As, vanadium (V), cadmium (Cd), and cobalt (Co), have been reported to induce carcinogenesis both in animals and in humans, the underlying mechanisms are not well understood. Since carcinogenesis induced by metals involves a variety of facets, it is difficult to identify one common mechanism. It is very likely that each metal has its own unique molecular mechanisms which contribute to the cancer development.

During the last two decades, chemical and cellular studies have provided a variety of contributions to extend our understanding for metal-induced carcinogenesis. Generally, carcinogenesis is considered to have the following four stages: initiation, promotion, progression, and metastasis. Although

mutations on genome DNA which are capable of activating oncogenes or inactivating tumor suppressors, are traditionally considered to be the crucial factor for cancer initiation, other events, such as transcription activation, recombination, and oncogene amplification, which may or may not require DNA damage, also contribute to the tumor initiation process [3–7]. Altered gene expression and cell signaling are considered to be related to tumor promotion and progression [8, 9]. The mechanisms of metal-induced carcinogenesis are believed to be involved in all stages of cancer development.

Metal compounds are found to have effects on the cellular organelles and components, such as cell membrane, mitochondrial, lysosome, endoplasmic reticulum, nuclei, and some enzymes involved in metabolism, detoxification, and damage repair [10]. All these systems are considered to influence metal-induced cellular responses. Metal ions have been found to directly bind to some cell components such as DNA and nuclear proteins through ionic and coordination bonds, causing

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Molecular Mechanisms of Metal Toxicity and Carcinogenesis Xianglin Shi,Vince Castranova,Val Vallyathan,William G. Perry,2012-12-06 During the last two decades chemical and cellular studies have contributed enormously to our understanding of metal induced carcinogenesis and many hypotheses on the role of metals in pathophysiological processes have been investigated In addition new techniques are available to shed light on the mechanism of carcinogenesis in molecular terms This conference on Molecular Mechanisms of Metal Toxicity and Carcinogenesis in September 2000 focused on the latest research in molecular mechanisms of metal induced toxicity and carcinogenesis The conference promoted a multidisciplinary investigative approach and included presentations from international experts on state of the art information in this field *Molecular Mechanisms of Metal Toxicity and Carcinogenesis* Xianglin Shi,Vince Castranova,Val Vallyathan,William G. Perry,2012-12-15 These proceedings focus on the latest research in molecular mechanisms of metal induced toxicity and carcinogenesis The conference promoted a multidisciplinary investigative approach and included presentations from international experts on state of the art information in this field Molecular Mechanisms of Metal Toxicity and Carcinogenicity ,1994 **Molecular Mechanisms of Metal Toxicity and Carcinogenicity** ,2002

Molecular Mechanisms of Metal Toxicity and Carcinogenicity ,1994 *Environmental Health Perspectives* ,1993

Molecular Mechanisms of Metal Toxicity and Carcinogenicity ,1989 **Metal Toxicology Handbook** Debasis

Bagchi,Manashi Bagchi,2020-11-19 Heavy metals and metalloids singly or in combination induce toxic manifestations either through acute or chronic pathology In particular long term chronic exposure to diverse heavy metals and metalloids to humans and animals can lead to numerous physical muscular neurological nephrological and diverse degenerative diseases and dysfunctions including multiple sclerosis muscular dystrophy Parkinson s and Alzheimer s diseases cardiovascular disorders and several others Recognized heavy metals such as lead mercury arsenic cadmium thallium and hexavalent chromium are known for enormous toxicity The immediate vital signs of acute heavy metal exposure include nausea vomiting diarrhea and acute abdominal pain Mercury has been identified as the most toxic heavy metal and mercury poisoning is known as acrodynia or pink disease Similarly lead another toxic heavy metal was at one time an integral part of painting Metal Toxicology Handbook further explains and discusses the varying attributes of metals discussing toxicity safety and proper human utilization of metals Beginning with a broad overview of metals metalloids redox biology and neurodegeneration and going further into the roles benefits and toxicity of metals with each section the text contains 28 chapters from eminent researchers and scientists in their respective fields and is a must have for anyone researching the potential toxicity in metals Key Features Discusses the pathology of metal toxicity Highlights the benefits of metals Explains the mechanism and salient features of restoring metabolic homeostasis Highlights dose dependent beneficial and adverse

effects of vanadium safety and toxicity The initial introductory section provides a broad overview of metals metalloids redox biology and neurodegeneration The second section discusses the pathology of metal toxicity in two chapters while the third section highlights the mechanism and salient features of restoring metabolic homeostasis in two chapters The fourth section demonstrates the aspect of radionuclides toxicity In a change of pace the fifth section discusses the benefits of metals in four chapters The sixth section titled Toxic Manifestations by Diverse Heavy Metals and Metalloids provides fourteen chapters that discuss the toxicological mechanism and manifestation of individual metals The editors have crafted a commentary titled A Treatise on Metal Toxicity and summarized a vivid scenario of metal toxicity and its consequences Cancer: Cell Structures, Carcinogens and Genomic Instability Leon P. Bignold, 2006-01-27 This volume began with an invitation from the publishers to edit a volume of EXS on Cancer This invitation undoubtedly derived from my articles in Cellular and Molecular Life Sciences in 2002 and 2003 on the relationships between the morphology aetiology and pathogenesis of tumours especially in relation to genetic instability After many years of teaching the theories of cancer in undergraduate medical school courses it seemed to me that the variably chaotic histopathologic features of tumours parallel in some way the variably unstable genomes of tumour cells which were being discovered in the 1990s Thus the title of the volume has come to include morphology carcinogenesis and genetic instability The invitation came while I was working with Herrn Dr med Hubertus Jersmann MD D sseldorf PhD now Senior Lecturer in Medicine of the University of Adelaide and Professor Brian Coghlan Emeritus Professor of German the University of Adelaide on the work of the nineteenth century cancer pathologists especially David Paul von Hansemann 1858 1920 With the delivery of the manuscripts from the authors of the chapters it became obvious that a background chapter for the volume could include some of the material which we had uncovered together Because of this chapter 1 is authored by the three of us and the new material figures prominently

Environmental Health Perspectives Supplements ,1994 *Benzene Toxicity, Carcinogenesis, and Epidemiology* Robert Snyder,1996 **Oxygen/nitrogen Radicals and Cellular Injury** Kenneth B. Adler,Robert D. Devlin,Val Vallyathan,1998 *Special Reports* Robert Snyder,1993 **Radiation and Human Health** Michael R. Quastel,John R. Goldsmith,1997 **Alternative Testing Methodologies** ,1998 *Integrated Approaches for Studying Hazardous Substances* William Alfred Suk,1998 *Cumulated Index Medicus* ,1991 *Networking of Mutagens in Environmental Toxicology* Kavindra Kumar Kesari,2019-05-25 This book covers the latest environmental issues based on current research objectives All chapters are fundamentally interlinked and focus on deciphering the networking of mutagens in environmental toxicity and human health Our changing environment climate and lifestyle factors are growing concerns in the 21st century The existing mutagens either physical or chemical are responsible for environmental toxicity These toxicants are carcinogenic and not limited to naturally occurring chemicals or biologicals but can also be man made such as radiation The networking of mutagens can have a broad range of effects on both the environment and human health Accordingly the

respective chapters explore the networking of mutagens in connection with environmental toxicity and address 1 Extant types of man made radiation and their effects on the environment and biological systems2 Heavy metal contaminations Effects on environmental health3 Networking of environmental pollutants in the air dust soil water and natural toxins in the environment Exposure and health4 The molecular interaction of environmental carcinogens with DNA An oncoinformatics approach5 Fundamentals of nonotoxicity carcinogenicity mutagenic and neurotoxicity in environmental health6 The role of antioxidants and medicinal plants in reducing the impacts of disease causing pollutants A sequel to Perspectives in Environmental Toxicology this book highlights the latest developments in the field of environmental toxicology It offers a valuable resource for researchers scholars and graduate students alike Occupational Cancer in Europe ,1999

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