

# Paraoxonase (PON1) in Health and Disease: Basic and Clinical Aspects

Edited by  
Lucio G. Costa  
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# Paraoxonase Pon1 In Health And Disease Basic And Clinical Aspects

**Srinivasa T. Reddy**



## **Paraoxonase Pon1 In Health And Disease Basic And Clinical Aspects:**

Paraoxonase (PON1) in Health and Disease Lucio G. Costa, Clement E. Furlong, 2002-11-30 The journey to find genes responsible for determining sensitivity or resistance to specific insecticides led to the paraoxonase PON1 gene on human chromosome 7 This gene encodes a 355 amino acid protein that is localized on the high density lipoprotein HDL particles in plasma Characterization of this gene revealed that different individuals expressed both different forms of this enzyme with amino acid substitutions at positions 55 and 192 as well as different levels of this protein Additional studies showed that mutations in the regulatory region of the PON1 gene contributed to the very different levels of plasma PON1 among individuals It turned out that both the level of the enzyme as well as the amino acid present at position 192 glutamine or arginine are important in determining resistance to the active forms of specific organophosphorus insecticides especially diazinon and chlorpyrifos The position 192 amino acid also determined whether an individual's plasma hydrolyzed the nerve agents soman and sarin at high or low rates It is not yet known whether these different rates of hydrolysis observed in biochemical assays reflect differences in sensitivity of individuals to nerve agents Taken together all of the experiments carried out to date indicate that engineered recombinant PON1 is an excellent candidate to use for treating cases of poisoning by specific organophosphorus compounds The available data on the relationship of PON1 levels and position 192 genotype led us to introduce the term PON1 status to describe an individual's PON1 plasma level as well as their position 192 genotype The characterization of the genetic variations of the PON1 gene together with experiments showing that HDL can protect the lipids in low density lipoprotein particles LDL from oxidation and that it was PON1 that was responsible for this protection have opened an entirely new area of investigation the role of PON1 in protecting against vascular disease More recent reports have noted that PON1 also metabolizes a number of drugs activating some and inactivating others This book describes the recent advances in understanding the role of PON1 in both cardiovascular disease and toxicology of insecticide exposure as well as some of the recent information indicating an important possible role in the pharmacokinetics of drug metabolism The final chapter of the book provides an overview of the areas of PON1 research and suggests future directions for research on PON1 as well as the related linked genes PON2 and PON3

**Paraoxonase (PON1) in Health and Disease** Lucio G. Costa, Clement E. Furlong, 2012-12-06 The paraoxonase or PON family of genes resides on human chromosome 7q2t 22 in the order PONT PON3 and PON2 PONT was one of the early genes identified as an environmentally relevant gene in that it is important in determining an individual's sensitivity or resistance to exposure from specific organophosphorus OP insecticides Paraoxonase PONT is an A esterase i e not inhibited by OP compounds initially identified for its ability to catalytically hydrolyze paraoxon the toxic metabolite oxon form of the insecticide parathion Evidence accumulated in the past several years has established that this enzyme which is present at variable levels in liver and serum of different individuals is an important determinant of sensitivity to toxicity of specific organophosphorus compounds

including chlorpyrifos oxon and diazoxon Recent experiments have pointed out that it is the catalytic efficiency of PONT together with the levels of PONT that are important in determining the degree of resistance Surprisingly even though PONT has a higher catalytic efficiency than PONTQ 92 for paraoxon RJ92 hydrolysis it does not provide significant in vivo protection against an exposure to paraoxon Interest in this enzyme has also emerged from the finding that it displays genetic polymorphisms in most populations with a significant number of the individuals in a given population carrying a PONT gene that puts them at risk for a specific OP exposure Paraoxonase (Pon1) in Health and Disease Lucio G Costa, Clement E Furlong, 2002-11-30

**The Paraoxonases: Their Role in Disease Development and Xenobiotic Metabolism** Bharti Mackness, Mike Mackness, Michael Aviram, György Paragh, 2007-10-26 In September 2006 the 2nd International Conference on Paraoxonases took place in Hajd szoboszl Hungary bringing together the world's foremost experts in the field The current book is a distillation of the plenary lectures which took place at the meeting resulting in a comprehensive up to date state of the art review of current paraoxonase research The book details a unique and novel enzyme whose physiological pathological functions are just starting to be revealed **Handbook of Toxicology of Chemical Warfare Agents** Ramesh C

Gupta, 2015-01-21 Handbook of Toxicology of Chemical Warfare Agents Second Edition covers every aspect of deadly toxic chemicals used in conflicts warfare and terrorism Including findings from experimental as well as clinical studies this essential reference offers in depth coverage of individual toxicants target organ toxicity major incidents toxic effects in humans animals and wildlife biosensors and biomarkers on site and laboratory analytical methods decontamination and detoxification procedures and countermeasures Expanding on the ground breaking first edition Handbook of Toxicology of Chemical Warfare Agents has been completely updated presenting the most recent advances in field Brand new chapters include a case study of the Iran Iraq war an overview of chemical weapons of mass destruction explosives Ricin the human respiratory system alternative testing methods brain injuries and more Unites world leading experts to bring you cutting edge agent specific information on Chemical Warfare Agents CWA and their adverse effects on human and animal health and the environment Provides you with all the information you need on CWA modes of action detection prevention therapeutic treatment and countermeasures New to this edition a full update to reflect the most recent advances in the field and new chapters on emergency preparedness the chemical warfare agents used in Syria and the use of the Novichok agent in the UK

**Environmental Health Perspectives**, 2004 Toxicology of Organophosphate and Carbamate Compounds Ramesh C Gupta, 2011-04-28 This text reference book provides the most comprehensive coverage of anticholinesterase compounds Organophosphates and Carbamates which constitute the largest number of chemicals that are primarily used as insecticides in agriculture industry and around the home garden Some OPs nerve agents have been used in chemical warfare and terrorist attacks while some OPs and CMs have been recommended as therapeutic agents in human medicine as well as in veterinary medicine Many chemicals of both classes are extremely toxic and lack selectivity thus their inadvertent accidental

use continues to pose a threat to human and animal health aquatic systems and wildlife These anticholinesterase agents produce a variety of toxicological effects in target and nontarget organs In light of this complexity this multi authored book is written by the well known scientists from many countries The book is organized into nine sections with a total of 49 chapters to provide in depth knowledge on various aspects of OP and CM compounds including their use classification mechanism based toxicity and prophylactic and therapeutic measurements Several chapters are written with special emphasis to cover timely topics such as chemical warfare agents physiologically based pharmacokinetic modeling structure and function of cholinesterases paraoxonase carboxylesterases developmental neurotoxicity the intermediate syndrome oxidative stress endocrine disruption and DNA damage gene expression and carcinogenesis Section VI with 5 chapters is specifically devoted to risk assessment and safety and regulatory guidelines for pesticides Describes everything you need to know about Organophosphates and Carbamates Extensively covers pesticides nerve agents therapeutic drugs and flame retardants Describes epidemiology of the world s major disasters involving Organophosphates and Carbamates Covers animal human aquatic and wildlife toxicity of Anticholinesterases Insights into in depth cholinergic and noncholinergic mechanisms of toxicity Describes recent advancements in cholinesterases paraoxonases carboxylesterases oxidative stress endocrine disruption cardiac and pulmonary toxicity and carcinogenesis Provides in vitro and in vivo models for neurotoxicity testing Integrates knowledge of studies in lab animals and humans Offers risk safety assessment and national international guidelines for permissible levels of pesticide residues Describes management of Anticholinesterase poisoning in humans

**Neurotoxicity of Metals** Michael Aschner, Lucio G. Costa, 2017-09-09 Assembles international authorities to address contemporary research in metal neurotoxicity Essential and non essential metals play an important role in neurodevelopmental and neurodegenerative diseases Recent developments in understanding the role of metals in the etiology of these disorders have led to rapid growth in clarifying the pathology of some of the most devastating diseases we face and in identifying potential new therapies Few books or periodicals have been wholly dedicated to the topic of metals and this collection is intended to serve as a resource for all researchers interested in metals and their role in health and disease Paraoxonases in Inflammation, Infection, and Toxicology Srinivasa T. Reddy, 2010-03-11 This series does not include back cover copy

**Anticholinesterase Pesticides** Tetsuo Satoh, Ramesh C. Gupta, 2011-03-25 This book offers an important reference source about the most common classes of pesticides for researchers engaged in the area of neurotoxicology metabolism and epidemiology The book presents details about thorough characterization of target and non target enzymes and proteins involved in toxicity and metabolism and epidemiology of poisonings and fatalities in people from short and long term exposures to these pesticides in different occupational settings on an individual country basis as well as on a global basis The early portion of the book deals with metabolism mechanisms and biomonitoring of anticholinesterase pesticides while the later part deals with epidemiological studies regulatory issues and therapeutic intervention

**Implications of lipids and modified lipoproteins in atherogenesis: From mechanisms towards novel diagnostic and therapeutic targets** Alexander Akhmedov, Chu-Huang Chen, Tatsuya Sawamura, 2023-08-01

**The HDL Handbook** Tsugikazu Komoda, 2010-09-06 The HDL Handbook Biological Functions to Clinical Implications brings laboratory research in HDL from bench to bedside in this needed resource for researchers and clinicians studying cholesterol lipids epidemiology biochemistry molecular medicine and pathophysiology of cardiovascular diseases In addition researchers and clinicians working with an aging population corporate researchers post doctorates medical students and graduate students will find this publication useful because the scope of coverage includes basic science genetics epidemiology and treatment of HDL cholesterol as well as potential targets to modify HDL cholesterol Comprehensive coverage of basic science genetics epidemiology and treatment Reputable content on latest advances in HDL cholesterol research Inclusive worldwide content with country specific information In depth discussion of potential targets to modify HDL

**Genomic and Personalized Medicine**, 2012-10-30 Genomic and Personalized Medicine Second Edition winner of a 2013 Highly Commended BMA Medical Book Award for Medicine is a major discussion of the structure history and applications of the field as it emerges from the campus and lab into clinical action As with the first edition leading experts review the development of the new science the current opportunities for genome based analysis in healthcare and the potential of genomic medicine in future healthcare The inclusion of the latest information on diagnostic testing population screening disease susceptibility and pharmacogenomics makes this work an ideal companion for the many stakeholders of genomic and personalized medicine With advancing knowledge of the genome across and outside protein coding regions of DNA new comprehension of genomic variation and frequencies across populations the elucidation of advanced strategic approaches to genomic study and above all in the elaboration of next generation sequencing genomic medicine has begun to achieve the much vaunted transformative health outcomes of the Human Genome Project almost a decade after its official completion in April 2003 Highly Commended 2013 BMA Medical Book Award for Medicine More than 100 chapters from leading researchers review the many impacts of genomic discoveries in clinical action including 63 chapters new to this edition Discusses state of the art genome technologies including population screening novel diagnostics and gene based therapeutics Wide and inclusive discussion encompasses the formidable ethical legal regulatory and social challenges related to the evolving practice of genomic medicine Clearly and beautifully illustrated with 280 color figures and many thousands of references for further reading and deeper analysis

**Human Genome Epidemiology** Muin J. Khoury, Julian Little, Wylie Burke, 2004 This book describes the important role that epidemiologic methods play in the continuum from gene discovery to the development and application of genetic tests It proceeds systematically from the fundamentals of genome technology and gene discovery to epidemiologic approaches to gene characterization in the population to the evaluation of genetic tests and their use in health services

**Human Developmental Neurotoxicology** David C. Bellinger, 2006-04-06 This reference describes the most

recent developments in the design execution and interpretation of human developmental neurotoxicology studies Assessing critical issues and controversies in the field this guide focuses on dose response effect relationships and explores challenges in the measurement of exposure to different types of chemicals *Toxicology for the Health and Pharmaceutical Sciences* Antonio Peña-Fernández, Mark D. Evans, Marcus S. Cooke, 2021-12-21 There is an increasing need for knowledge of toxicology to safeguard the use of chemicals in industry and in the public and private sectors The study of toxicology is becoming increasingly relevant in human health sciences as future health and clinical professionals will be pivotal in addressing and managing emerging chemical threats and hazards related to modern anthropogenic activities and technological development Comprising a series of chapters from leading toxicology pharmacy and public health academics and experts across Europe the United States and beyond *Toxicology for the Health and Pharmaceutical Sciences* provides a concise yet comprehensive volume that can be used as a relevant textbook on toxicology for the clinical healthcare educational and professional sectors Key Features Includes cutting edge information regarding the very latest environmental threats to public health Provides a detailed case study based on a real world scenario that allows the reader to practice human health risk assessment Describes innovative guidance and tools to respond to chemical incidents and attacks which enables the reader to tailor an effective protection and remediation response This book covers the fundamentals and recent developments in toxicology to respond to local and global chemical pharmaceutical and environmental threats Thus this volume has chapters specifically designed to support the understanding of the most current toxicology related subjects for any undergraduate postgraduate health programs as well as aid the delivery of continuing professional development training on up to date topics in toxicology for current practicing health professionals wishing to improve their background knowledge in toxicology The book is also vital reading and reference for policy makers and others that influence and set regulations that have an impact on the environment and human health **Omega-3 Fatty Acids** Mahabaleshwar V. Hegde, Anand Arvind Zanwar, Sharad P.

Adekar, 2016-09-15 This volume argues for the importance of essential nutrients in our diet Over the last two decades there has been an explosion of research on the relationship of Omega 3 fatty acids and the importance of antioxidants to human health Expert authors discuss the importance of a diet rich in Omega 3 Fatty acids for successful human growth and development and for the prevention of disease Chapters highlight their contribution to the prevention and amelioration of a wide range of conditions such as heart disease diabetes arthritis cancer obesity mental health and bone health An indispensable text designed for nutritionists dietitians clinicians and health related professionals *Omega 3 Fatty Acids Keys to Nutritional Health* presents a comprehensive assessment of the current knowledge about the nutritional effects of Omega 3 fatty acids and their delivery in foods **Anti-atherogenic Properties of Paraoxonase 2 and Paraoxonase 3** Carey Jene Ng, 2004 *10 Years of Pharmacogenetics and Pharmacogenomics* Jose Agundez, 2020-07-08 The Specialty Section Pharmacogenetics and Pharmacogenomics makes part of two different Journals *Frontiers in Pharmacology* and *Frontiers in*

Genetics This Specialty Section focuses on the mechanisms by which genetic variations influence drug effects and adverse drug events and cover basic research clinical translation applications in drug development and regulatory issues related to this field Also studies addressing the role of other factors such as epigenetics phenotypic factors or drug drug interactions on drug pharmacokinetics or pharmacodynamics are welcome The editorial board is composed of 34 Associate Editors which together with the Guest Associate Editors and the Reviewer Editors constitute a team of nearly 340 leading experts in the field of Pharmacogenetics and Pharmacogenomics This guarantees high quality in the reviewing process as well as short review times A look back 10 years of Frontiers in Pharmacogenetics Pharmacogenomics Continued in eBook

**Pesticides in the Modern World** Margarita Stoytcheva, 2011-09-12 The introduction of the synthetic organochlorine organophosphate carbamate and pyrethroid pesticides by 1950 s marked the beginning of the modern pesticides era and a new stage in the agriculture development Evolved from the chemicals designed originally as warfare agents the synthetic pesticides demonstrated a high effectiveness in preventing destroying or controlling any pest Therefore their application in the agriculture practices made it possible enhancing crops and livestock s yields and obtaining higher quality products to satisfy the food demand of the continuously rising world s population Nevertheless the increase of the pesticide use estimated to 2 5 million tons annually worldwide since 1950 created a number of public and environment concerns This book organized in two sections addresses the various aspects of the pesticides exposure and the related health effects It offers a large amount of practical information to the professionals interested in pesticides issues



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