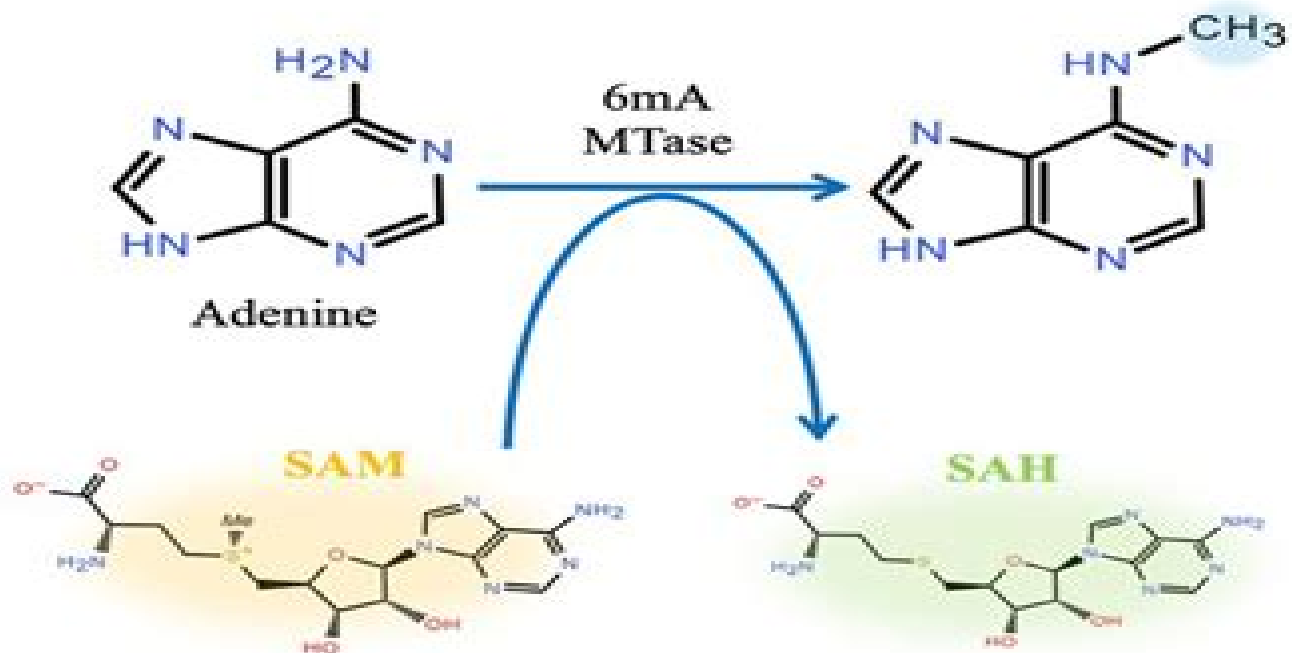
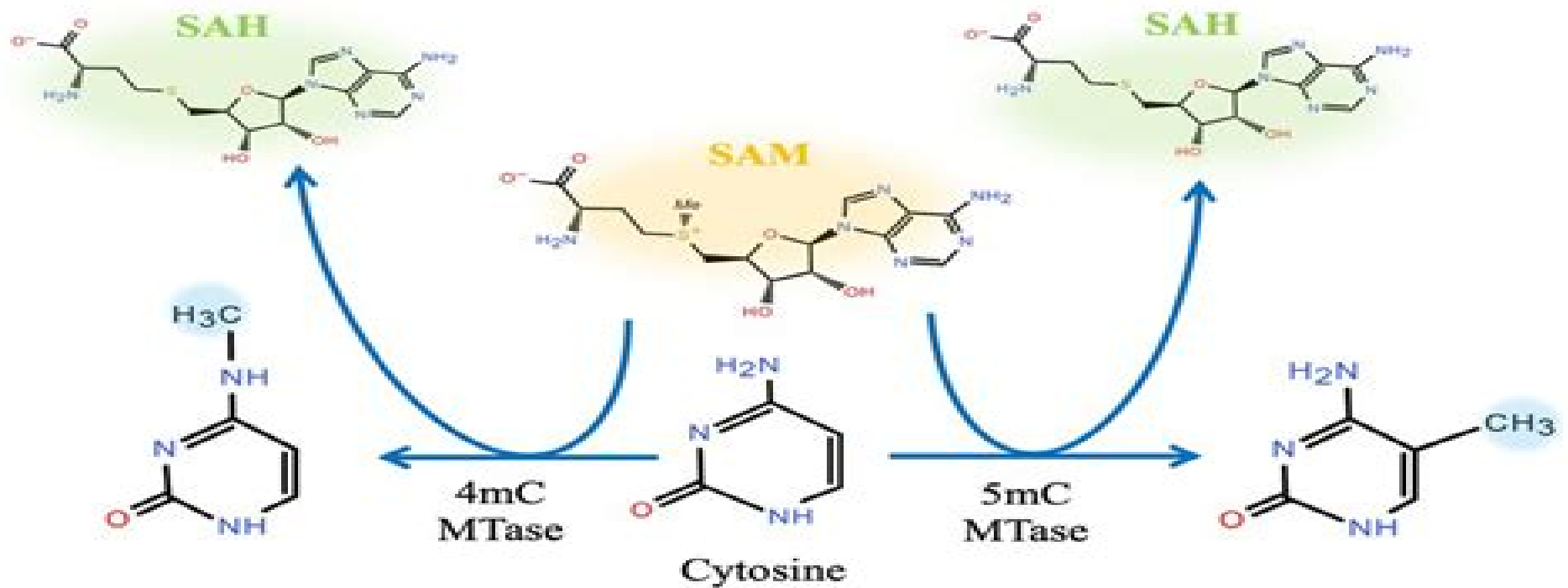




Sadenosylmethioninedependent Methyltransferases

Xiaodong Cheng, Robert Blumenthal



Sadenosylmethionine-independent Methyltransferases:

S-adenosylmethionine-dependent Methyltransferases Xiaodong Cheng, Robert Blumenthal, 1999 This invaluable volume written by an international group of scientists presents an overview of the AdoMet dependent methyltransferases with special emphasis on structure function relationships S adenosyl L methionine AdoMet is the second most commonly used enzyme cofactor after ATP The AdoMet dependent methyltransferases act on a wide variety of target molecules including DNA RNA protein polysaccharides lipids and a range of small molecules The well conserved architecture of these enzymes and the implications of this conservation for their evolutionary history are major themes of this book The thirteen chapters describe in detail the structures enzyme kinetics and biological roles of the AdoMet dependent methyltransferases from a wide range of cell types plant animal bacterial and archaeal *Regulatory Roles of S-adenosylmethionine-dependent O-methyltransferases* Kelley L. Banfield, 2004 *Biochemistry of S-adenosylmethionine and Related Compounds* Earl Usdin, 2016-01-01 **Comprehensive Natural Products III**, 2020-07-22 Comprehensive Natural Products III Third Edition Seven Volume Set updates and complements the previous two editions including recent advances in cofactor chemistry structural diversity of natural products and secondary metabolites enzymes and enzyme mechanisms and new bioinformatics tools Natural products research is a dynamic discipline at the intersection of chemistry and biology concerned with isolation identification structure elucidation and chemical characteristics of naturally occurring compounds such as pheromones carbohydrates nucleic acids and enzymes This book reviews the accumulated efforts of chemical and biological research to understand living organisms and their distinctive effects on health and medicine and to stimulate new ideas among the established natural products community Provides readers with an in depth review of current natural products research and a critical insight into the future direction of the field Bridges the gap in knowledge by covering developments in the field since the second edition published in 2010 Split into 7 sections on key topics to allow students researchers and professionals to find relevant information quickly and easily Ensures that the knowledge within is easily understood by and applicable to a large audience **Marine Enzymes and Specialized Metabolism - Part A**, 2018-05-17 Marine enzymes and specialized metabolism Part A Volume 604 highlights experimental methods on diverse marine enzymes involved in the construction of bioactive natural product molecules These detailed protocols are written by experts who actively study and apply marine enzymes in biosynthesis and biotechnology Comprehensive chapters in this latest release cover Chemoenzymatic synthesis of starting materials and characterization of halogenases requiring acyl carrier protein tethered substrates Assaying biradical aryl coupling activity of CYP450 enzymes the Characterization and application of marine microbial omega 3 polyunsaturated fatty acid synthesis Catalase related allene oxide synthase on a biosynthetic route to fatty acid cyclopentenones Haloalkane dehalogenases from marine microorganisms and more Presents comprehensive information on a subject not widely covered in other method book Contains the authority and expertise of recognized and celebrated contributors Structural Studies

of the S-Adenosylmethionine-Dependent Methyltransferases Yi Peng, 2009 S adenosylmethionine dependent methyltransferases AdoMet dependent MTases are a main subfamily of MTases which play critical roles in diverse methylation reactions in many significant biological processes AdoMet dependent MTases catalyze methylation reactions utilizing the methyl donor AdoMet This thesis describes structure function studies of several members of this enzyme family which are biomedically important By combining experimental X ray crystallography and theoretical molecular dynamics simulation calculations structural biology techniques with molecular biology and functional studies the work presented here provides molecular insight into mechanisms of enzyme function and drug response The first enzyme studied thiopurine S methyltransferase TPMT modulates the cytotoxic effects of thiopurine prodrugs such as 6 mercaptopurine 6MP by methylating them in a reaction using AdoMet as the donor Patients with TPMT variant allozymes exhibit diminished levels of protein and or enzyme activity and are at risk for thiopurine drug induced toxicity We have determined two crystal structures of wild type murine TPMT as a binary complex with the product S adenosyl L homocysteine AdoHcy and as a ternary complex with AdoHcy and the substrate 6MP to 1.8 and 2.0 resolution respectively Comparison of the structures reveals that an active site loop becomes ordered upon 6MP binding The positions of the two ligands are consistent with the expected SN2 reaction mechanism Arg147 and Arg221 the only polar amino acids near 6MP are highlighted as possible participants in substrate deprotonation Structure based mutagenesis and enzyme activity assays suggest that either Arg152 or Arg226 may participate in some fashion in the TPMT reaction with one residue compensating when the other is altered and that Arg152 may interact with substrate more directly than Arg226 consistent with observations in the murine TPMT crystal structure In addition we have compared the catalytic activity of wild type and 5 variant TPMTs and found that the variant s binding affinity for its methyl acceptor and donor substrates are reduced 10 fold and 2 fold contributing to decreased enzyme activity of murine TPMT 5 We have determined two crystal structures of murine TPMT 5 as a binary complex with AdoHcy and as a ternary complex with AdoHcy and 6MP respectively The TPMT 5 crystal structures together with molecular dynamics simulation calculations reveal that the active site loop is more flexible in TPMT 5 which affects the AdoMet and 6MP substrate affinity and results in loss of the enzyme activity In addition these TPMT 5 crystal structures and the computational modeling of other TPMT variants using wild type murine TPMT structures aid our understanding of the molecular consequences of TPMT polymorphisms Furthermore crystal structures of TPMT complexes with benzoic acid inhibitors and thiophenol substrate reveal that TPMT possesses a flexible active site which can accommodate both a smaller acceptor substrate such as thiophenol and larger benzoic acid inhibitors These structures provide insights into the connection between the subtle variation in binding of different acceptor substrate site ligands to TPMT and the different degree of inhibition by these benzoic acid inhibitors The structural features of the acceptor binding site characterized by the ensemble of TPMT structures reported here may be useful in identifying new small molecule modulators for optimization of thiopurine

based therapy Nicotinamide N methyltransferase NNMT catalyzes the N methylation of nicotinamide pyridines and other structural analogs using AdoMet as methyl donor The crystal structure of human NNMT which plays a significant role in the regulation of metabolic pathways and cancers was solved as the ternary complex bound to both AdoHcy and nicotinamide The structure reveals the structural basis for nicotinamide binding highlights several residues in the active site which may play roles in nicotinamide recognition and NNMT catalysis and provides a structural basis for the design of NNMT mutants to further investigate the enzyme s catalytic mechanism The structure based mutagenesis of NNMT is being pursued in ongoing studies Arsenic methyltransferase AS3MT is the third important AdoMet dependent MTase included in our studies It is involved in methylation of inorganic arsenic and relevant to public health To obtain the crystal structure of AS3MT for elucidation of the mechanism of arsenic methylation and to probe the relationship between AS3MT polymorphisms and individual variation in arsenic metabolism a number of AS3MT constructs have been prepared and characterized and efforts to crystallize AS3MT are ongoing

Characterization, Properties and Applications Tracey Rouault, 2017-08-21 This volume on iron sulfur proteins includes chapters that describe the initial discovery of iron sulfur proteins in the 1960s to elucidation of the roles of iron sulfur clusters as prosthetic groups of enzymes such as the citric acid cycle enzyme aconitase and numerous other proteins ranging from nitrogenase to DNA repair proteins The capacity of iron sulfur clusters to accept and delocalize single electrons is explained by basic chemical principles which illustrate why iron sulfur proteins are uniquely suitable for electron transport and other activities Techniques used for detection and stabilization of iron sulfur clusters including EPR and Mossbauer spectroscopies are discussed because they are important for characterizing unrecognized and elusive iron sulfur proteins Recent insights into how nitrogenase works have arisen from multiple advances described here including studies of high resolution crystal structures

Iron-Sulfur Clusters in Chemistry and Biology Tracey Rouault, 2014-08-20 This volume on iron sulfur proteins includes chapters that describe the initial discovery of iron sulfur proteins in the 1960s to elucidation of the roles of iron sulfur clusters as prosthetic groups of enzymes such as the citric acid cycle enzyme aconitase and numerous other proteins ranging from nitrogenase to DNA repair proteins The capacity of iron sulfur clusters to accept and delocalize single electrons is explained by basic chemical principles which illustrate why iron sulfur proteins are uniquely suitable for electron transport and other activities Techniques used for detection and stabilization of iron sulfur clusters including EPR and Mossbauer spectroscopies are discussed because they are important for characterizing unrecognized and elusive iron sulfur proteins Recent insights into how nitrogenase works have arisen from multiple advances described here including studies of high resolution crystal structures Numerous chapters discuss how microbes plants and animals synthesize these complex prosthetic groups and why it is important to understand the chemistry and biogenesis of iron sulfur proteins In addition to their vital importance in mitochondrial respiration numerous iron sulfur proteins are important in maintenance of DNA integrity Multiple rare human diseases with different clinical presentations

are caused by mutations of genes in the iron sulfur cluster biogenesis pathway Understanding iron sulfur proteins is important for understanding a rapidly expanding group of metabolic pathways important in all kingdoms of life and for understanding processes ranging from nitrogen fixation to human disease

Conjugation—Deconjugation Reactions in Drug Metabolism and Toxicity Frederick C. Kauffman, 2012-12-06 Advances in molecular biology describing important enzyme systems involved in drug conjugation and deconjugation reactions and recent work indicating the importance of drug and xenobiotic conjugates as transport forms of biologically active compounds are reviewed comprehensively Part One describes molecular events associated with the expression and regulation of transferases and hydrolases involved in Phase II drug conjugation and deconjugation Part Two deals with the regulation of Phase II conjugation and Part Three reviews critically the importance of drug conjugates in pharmacology and toxicology This volume is an up to date source of information on this topic and will be of broad interest to pharmacologists and toxicologists

Cumulated Index Medicus, 1994

Red Blood Cell Aging Antonio De Flora, Mauro Magnani, 2013-03-08 The mammalian erythrocyte is a very suitable model for the study of aging at the cellular and molecular level It is not only a matter of apparent simplicity in terms of biochemistry biophysics and physiology but more likely this cell offers a great possibility for elucidating some basic problems in the process of aging In fact nowadays it is possible to follow individual cells all along their life span in circulation it is possible to obtain these cells when young middle aged or old and it is possible to obtain cells from individuals of defined ages and transfuse them into compatible recipients to investigate the role of the environment where the cell lives and finally it is possible to easily manipulate the red cell content in terms of enzymatic activities and or metabolic properties to investigate the possible effect of these manipulations on cell survival This book *Red Blood Cell Aging* is based on a symposium held in Urbino Italy at the end of 1990 and examines the impact of age on the membrane metabolism structural and enzymatic proteins of mammalian erythrocytes The various contributions to this symposium not only described those processes of aging which affect the cell but also provided a nearly complete picture of the event s and mechanism s that every day permits to recognize among 25 trillion circulating red cells in an average adult that 1 percent that have reached the end of their 120 day life span in circulation

RNA Modification, 2015-12-11 RNA Modification provides a useful examination of the science and its role in biological regulation the current frontier of life science research and includes various RNA modifications and their role in gene expression It represents the most up to date knowledge and protocols available today Dynamic RNA modifications and their roles in biological regulation are the current frontier of life science research This volume of *Methods in Enzymology* represents up to date knowledge and protocols

Antiviral Drug Development Erik De Clercq, Richard T. Walker, 2012-12-06

Regulatory Mechanisms in Transcriptional Signaling, 2009-07-25 *Regulatory Mechanisms in Transcriptional Signaling* volume of *Progress in Molecular Biology and Translational Science* includes in depth discussion on roles of Chromatin remodeling proteins in nuclear receptor signaling and the ANCCA regulator in cancer

This important resource edited by Dr Debabrata Debu Chakravarti offers research on the progesterone receptor action in leiomyoma and endometrial cancer and emerging roles of the ubiquitin protein system in nuclear hormone receptor signaling to provide the reader with expert discussions of up to date research

Psychopharmacology Abstracts, 1974

Arsenic Exposure and Health Effects V W.R. Chappell, C.O. Abernathy, R.L. Calderon, D.J. Thomas, 2003-12-19 The authoritative articles in this book represent the state of the art in arsenic research Arsenic experts from around the world participants in the Fifth International Conference on Arsenic Exposure and Health Effects organized by the Society for Environmental Geochemistry and Health in 2002 present their critical findings The authors share their latest arsenic research findings in Occurrence Epidemiology Biomarkers and Animal Models Mode of Action Mode of Action Risk Estimation Intervention and Medical Treatment and Water Treatment and Remediation As in past conferences the first report of elevated arsenic exposures in a new country was given The Conference introduced the finding of arsenic contamination in Nepal and updates of the arsenic problems in Bangladesh India Vietnam are included A vital contribution to arsenic study and policy making this volume examines the global impact of the toxin and discusses arsenic in the environment mechanisms of arsenic metabolism and carcinogenesis water treatment technology and medical care Arsenic Exposure and Health Effects V offers informed challenging insights into a highly important and controversial topic

Protein Methylation Woon Ki Paik, Sangduk Kim, 2024-12-20 This significant volume provides reviews on protein methylation reactions which occur ubiquitously in nature Written in a comprehensive style this work covers knowledge on the natural occurrence of methylated amino acids their chemical synthesis plus the enzymology biological regulator and biological significance of free methylated amino acids It also includes various specific biological systems where posttranslational methylation reactions have been demonstrated This text is unique because the chapters are critically reviewed by authorities in each respective field This well written volume is an excellent reference to researchers as well as graduate students interested in post synthetic modifications of macromolecules

Secondary Metabolism in Microorganisms, Plants and Animals M. Luckner, 2013-12-11 Many of the reactions and compounds involved in metabolism are almost identical in the different groups of living organisms They are known as primary metabolic reactions and primary metabolic products In addition however a wide variety of biochemical pathways are characteristic of only a few species of organisms of single chemical races or even of a certain stage of differentiation of specialized cells Such pathways are collectively referred to as secondary metabolism and the compounds formed are called secondary products Secondary products are frequently revealed by their color smell or taste They are responsible for the flavor of most foodstuffs and beverages and for the color and fragrance of flowers and fruits Many of them are part of the materia medica e g alkaloids cardiac glycosides antibiotics or compounds acting as hormones Others are used by industry e g rubber tannins and cellulose This book treats the organization and significance of biosynthesis storage transformation and degradation of the most important groups of secondary products in microorganisms plants and animals It shows that the

formation of secondary products is a common characteristic of specialized cells brought about by the action of special enzymes encoded by specific genetic material. It demonstrates that the biosynthesis of secondary products is typically without significance for the individual producer cell but may play a decisive role in the development and function of the producer organism as a whole.

Enzyme Catalysis in Organic Synthesis, 3 Volume Set Karlheinz Drauz, Harald Gröger, Oliver May, 2012-03-26 This comprehensive three volume set is the standard reference in the field of organic synthesis catalysis and biocatalysis. Edited by a highly experienced and highly knowledgeable team with a tremendous amount of experience in this field and its applications, this edition retains the successful concept of past editions while the contents are very much focused on new developments in the field. All the techniques described are directly transferable from the lab to the industrial scale, making for a very application oriented approach. A must for all chemists and biotechnologists.

New Horizons in Nitrogen Fixation Rafael Palacios, Jaime Mora, William E. Newton, 2013-06-29 In order to understand a process as complex as nitrogen fixation and to be in a position to manipulate it for the benefit of mankind, researchers are now working at the frontiers of science in many different areas: protein structure and function, catalytic mechanisms, electron transfer processes, regulatory circuits and environmental sensing, metabolic integration, chemical communication between organisms, differentiation, genome structure and function, microbial ecology, plant physiology, plant molecular biology and agronomy. This volume represents a testimony to the advances in nitrogen fixation research that have been made and the contribution of these efforts to the solution of many other varied scientific problems. Limiting steps for future advances are analyzed and new horizons in nitrogen fixation research are proposed.

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