

Mechanisms of human DNA repair: an update

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Abstract

The human genome, comprising three billion base pairs coding for 30 000–40 000 genes, is constantly attacked by endogenous reactive metabolites, therapeutic drugs and a plethora of environmental mutagens that impact its integrity. Thus it is obvious that the stability of the genome must be under continuous surveillance. This is accomplished by DNA repair mechanisms, which have evolved to remove or to tolerate pre-cytotoxic, pre-mutagenic and pre-clastogenic DNA lesions in an error-free, or in some cases, error-prone way. Defects in DNA repair give rise to hypersensitivity to DNA-damaging agents, accumulation of mutations in the genome and finally to the development of cancer and various metabolic disorders. The importance of DNA repair is illustrated by DNA repair deficiency and genomic instability syndromes, which are characterised by increased cancer incidence and multiple metabolic alterations. Up to 130 genes have been identified in humans that are associated with DNA repair. This review is aimed at updating our current knowledge of the various repair pathways by providing an overview of DNA-repair genes and the corresponding proteins, participating either directly in DNA repair, or in checkpoint control and signaling of DNA damage.

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1. Introduction

Fifty years after discovery of the structure of DNA (Watson and Crick, 1953), DNA repair has become one of the most interesting topics in modern biology. The sequencing of the human genome (Lander et al., 2001; Venter et al., 2001) yielded a first overview of the huge number of proteins involved in the protection of the genome. Recently, two papers compiled data of ~130 human DNA repair genes, which were cloned and sequenced. Not all of them, however, have been characterised yet as to their function (Ronen and Glickman, 2001; Wood et al., 2001). DNA-repair genes can be

sub-grouped into genes associated with signaling and regulation of DNA repair on the one hand and on the other into genes associated with distinct repair mechanisms such as mismatch repair (MMR), base excision repair (BER), nucleotide excision repair (NER), direct damage reversal and DNA double-strand break (DSB) repair. Mutations in genes involved in DNA repair are responsible for the development of tumors and various hereditary diseases characterised by complex metabolic alterations (see Table 1).

DNA repair genes and their corresponding proteins are also responsible for the development of cytostatic drug resistance in tumour cells. Historical aspects pertaining to the field of DNA repair have recently been highlighted (Friedberg, 2003) and several reviews on different areas of DNA repair appeared (Hoeijmakers, 2001; Lehmann, 2002; Lindahl, 2001; Svejstrup, 2002;

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Cumulated Index Medicus, 1969 **Index Medicus**, 2004 Vols for 1963 include as pt 2 of the Jan issue Medical subject headings **Index of Conference Proceedings Received** British Library. Lending Division, 1981 **DNA-repair Mechanisms** H. Altmann, 1972 DNA Repair Mechanisms Philip Hanawalt, 2012-12-02 DNA Repair Mechanisms is an account of the proceedings at a major international conference on DNA Repair Mechanisms held at Keystone Colorado on February 1978 The conference discusses through plenary sessions the overall standpoint of DNA repair The papers presented and other important documents such as short summaries by the workshop session conveners comprise this book The compilation describes the opposing views those that agree and dispute about certain topic areas This book divided into 15 parts is arranged according to the proceedings in the conference The plenary sessions are grouped with the related workshop and poster manuscripts The first two parts generally tackle repair in terms of its identification and quantification as well as the models systems and perspectives it utilizes The following parts discuss the various types of repair including base excision nucleotide excision repair in bacteria excision repair in mammalian cells inducible error prone repair in prokaryotes and strand break repair in mammalian cells among others This reference material looks into the replicative bypass mechanisms in mammalian cells viral probes and hereditary repair defects It explains repair deficiency and human disease as well as mutagenesis and carcinogenesis The last part of this book deals with the consequences and effects of DNA repair This volume is a helpful source of reference for students teachers scientists and researchers in the different fields of genetics radiology biochemistry and environmental biology *DNA-repair Mechanism*, 1972 DNA-REPAIR MECHANISMS- PROCEEDINGS OF A SYMPOSIUM., **DNA-Repair Mechanisms** H. Altman, 1972 DNA Repair Mechanisms, 1978 **DNA Repair Mechanisms and Their Biological Implications in Mammalian Cells** M. Lambert, 2013-03-09 This volume contains edited contributions from the speakers at the NATO Advanced Research Workshop on DNA Repair Mechanisms and Their Biological Implications in Mammalian Cells held October 1 6 1988 at the Abbaye Royale de Fontevraud Fontevraud France The meeting was dedicated to Paul Howard Flanders Yale University New Haven CT 1919 1988 whose seminal contributions to the DNA repair field include the discovery of the excision repair pathway the elucidation of post replication repair in E coli the isolation of the *lexA* and *recC* mutants and his extensive work on the enzymology of *RecA* A plethora of recent developments in DNA repair mechanisms and related processes in mammalian cells have advanced our understanding of this field in a number of different areas and have given new emphasis to the ways these systems both resemble DNA repair processes in other groups of organisms in some respects yet are strikingly different from them in others Within the past decade there have been a number of international conferences on DNA damage and repair mechanisms but none has been focused on these processes in mammalian cells *Mechanisms of DNA Repair*, 2012-10-22 Written by research experts this volume of Progress in Molecular Biology and Translational Science focuses on current

science surrounding the mechanisms of DNA repair Contributions from leading authorities Informs and updates on all the latest developments in the field DNA Payam Behzadi,2021-05-19 DNA is the most important biomolecule ever discovered Indeed this molecule bears genetic information from one generation to another In this regard DNA bases have a key role in transferring genetic information and data safely However there are cellular genetic and environmental factors that may damage the different parts of DNA molecules These damages may result in mutations and cell death As such several DNA repair mechanisms have evolved Over three sections this book examines many of these mechanisms Correcting the Blueprint of Life Errol C. Friedberg,1997 A brief history of the discovery of the more important mechanisms by which cells respond to DNA damage The study which introduces the study of DNA mutagenesis and repair is aimed at advanced undergraduates or graduate students as well as researchers in a variety of fields **Molecular Mechanisms for Repair of DNA** Philip Hanawalt,2012-12-06 An age has passed in the 40 years since we first observed recovery from radiation damage in irradiated bacteria During the early 1930s we had been discussing the possibility of rapid changes after radiation exposure with Farring ton Daniels Benjamin Duggar John Curtis and others at the University of Wisconsin After working with living cells we had concluded that organisms receiving massive insults must have a wide variety of repair mechanisms available for restoration of at least some of the essential properties of the cell The problem was how to find and identify these recovery phenomena At that time I was working on a problem considered to be of great importance the existence of the so called mitogenetic rays Several hundred articles and a score of books had already appeared dealing with mitogenetic rays a type of radiation that was thought to exist in the shorter ultraviolet region Our search for mitogenetic rays necessitated the design of experiments of greatest sensitivity for the detection of ultraviolet It was vital that conditions be kept as constant as possible during exposure All the work was done at icewater temperature 3 5 C during and after exposure We knew that light was an important factor for cell recovery so all our experiments were done in dim light with the plated out cells being covered with dark cloth Our statements on the effect of visible light stimulated Kelner to search for photoreactivation as it was later called

DNA Repair Inna Kruman,2011-11-07 The book consists of 31 chapters divided into six parts Each chapter is written by one or several experts in the corresponding area The scope of the book varies from the DNA damage response and DNA repair mechanisms to evolutionary aspects of DNA repair providing a snapshot of current understanding of the DNA repair processes A collection of articles presented by active and laboratory based investigators provides a clear understanding of the recent advances in the field of DNA repair *DNA Damage and Repair in Human Tissues* Betsy M. Sutherland,Avril D. Woodhead,2012-12-06 Physical and chemical agents in the environment damage the DNA of humans and pose a major threat to human health today and to the genetic integrity of human populations Although studies on isolated DNA in vitro on prokaryotes on mammalian cells in culture and on laboratory animals have provided essential background information it is now possible to study DNA damage and repair in human tissues directly New techniques of high sensitivity especially those

not requiring radioactive labeling have made possible quantitation of DNA damage and repair as well as detection of residual unrepaired DNA lesions In recent years several investigators have taken up the challenge of studying damage and repair responses in humans and we have chosen that work as the special focus of this Symposium Major advances in understanding damage and responses in human skin in blood cells and in human internal organs indicate three major themes First DNA damage levels in human tissues depend not only on the initial exposures but also on the capacity of that tissue for repair of the specific lesion type Second repair in human tissues may differ quantitatively and qualitatively from that in human cells in culture

Mechanisms of DNA Damage and Repair Michael G. Simic, Lawrence Grossman, Arthur C. Upton, David S. Bergtold, 2013-11-21 This book is based on the papers presented at the conference on Mechanisms of DNA Damage and Repair Implications for Carcinogenesis and Risk Assessment held at the National Bureau of Standards on June 27 1985 This volume deals with mechanisms of DNA damage and repair at the molecular level consequences of unrepaired or misrepaired damage with major emphasis on carcinogenesis drugs which bind selectively to altered and potentially damaging DNA sequences and potential utilization of DNA damage as an endpoint for assessing risks of UV light ionizing radiations chemicals drugs and hazardous agents in foods Because the induction of mutations by radiation and genotoxic chemicals has been observed to follow one hit kinetics in some instances it is generally assumed that any level of exposure to a DNA damaging agent may increase the risk of genetic disease or cancer in an exposed population At the same time however there is evidence that although the DNA of living cells is continually damaged by natural background radiation free radicals and other naturally occurring processes most of the damage is normally repaired

DNA Repair Mechanisms Errol C. Friedberg, C. Fred Fox, Philip C. Hanawalt, 1978

DNA Repair Allison E. Thomas, 2010 The preservation of expected life span and longevity as well as the assurance of life succession among all species requires the integrity and faithful transcription of DNA A dedicated machinery of DNA repair factors is responsible for reversing DNA damage across the genome Efficient response to various effectors of DNA damage is also dependent on a complex network of sensors and mediators of stress signals which are upstream of DNA repair activation and together constitute components of the DNA damage response DDR This book reviews research on cell cycle checkpoints as essential mechanisms for safeguarding genome stability nucleotide excision repair NER which recognises and removes bulky DNA damage that leads to DNA double helix distortion and others

DNA Repair: Mechanisms and Clinical Significance Nas Wilson, 2021-11-16 The collection of processes required to identify and correct the damage in the DNA molecules is known as DNA repair DNA damage can be caused by metabolic activities and environmental factors Cells are not able to function properly if the integrity and accessibility of essential information gets corrupted by DNA damage So to restore the correct information various strategies have been evolved according to the type of damage occurred in the double helical structure of DNA Some of these mechanisms are single strand damage double strand breaks direct reversal and translesion synthesis In single strand damage

one of the two strands of the double helix has a defect and the other strand can be used as a template to correct the defect This book aims to shed light on some of the unexplored aspects of DNA repair and the recent researches in this field It traces the progress of this field and highlights some of its key concepts This book will provide comprehensive knowledge to the readers

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