Human Mitochondrial Dna And The Evolution Of Homo Sapiens Nucleic Acids And Molecular Biology

Mitochondrial replacement techniques (MRTs) are designed to prevent the transmission of mitochondrial DNA (mtDNA) diseases from mother to child. While MRTs, if effective, could satisfy a desire of women seeking to have a genetically related child without the risk of passing on mtDNA disease, the technique raises significant ethical and social issues. It would create offspring who have genetic material from two women, something never sanctioned in humans, and would create mitochondrial changes that could be heritable (in female offspring), and therefore passed on in perpetuity. The manipulation would be performed on eggs or embryos, would affect every cell of the resulting individual, and once carried out this genetic manipulation is not reversible. Mitochondrial Replacement Techniques considers the implications of manipulating mitochondrial content both in children born to women as a result of participating in these studies and in descendants of any female offspring. This study examines the ethical and social issues related to MRTs, outlines principles that would provide a framework and foundation for oversight of MRTs, and develops recommendations to inform the Food and Drug Administration's consideration of investigational new drug applications.

Advances in information technology and next generation sequencing have propelled the

use of bioinformatics in agriculture, especially in the area of crop improvement. An extremely large amount of genomics data is available from plants and animals due to tremendous improvements in the field. This book acquaints readers with state-of-the-art sequencing technologies, recent developments in computing algorithms, and certain biological perspectives that influence development of bioinformatics tools by giving specific examples from model plant species. The challenge is now to make sense and use of this wealth of data.

This collection of reviews and protocols provides the reader with an introduction to the current state of knowledge on how various diseases are related to mitochondrial dysfunction. Mitochondria contain their own genome, a small, circular double-stranded DNA (mtDNA), and alterations in mtDNA may play an important role in the multistep carcinogenesis of at least some types of human cancer. In addition to mutations of mtDNA, many mitochondrial syndromes are due to abnormalities in nuclear genes related to oxidative phosphorylation (OXPHOS). Mitochondrial tRNA (MTT) gene mutations are an important cause of human morbidity and are associated with a wide range of pathology, from isolated organ?]specific diseases such as myopathy or hearing loss, to multisystem disorders with encephalopathy, gastrointestinal dysmotility, and life?]threatening cardiomyopathy. The relationship of the mitochondrion organelle to aging and longevity is also discussed. Laboratory protocols describe methodology to characterize mtDNA heteroplasmy by parallel sequencing. Each eukaryotic cell

contains hundreds of mitochondria with hundreds of mitochondria genomes. Mutant and wild-type mtDNA may co-exist as heteroplasmy, and cause human disease. The purpose of this protocol is to simultaneously determine mtDNA sequence and quantify the heteroplasmic level. Another protocol describes procedures for obtaining tissue sections and cell material suitable for histological evaluation of OXPHOS activity and integrity and immunodetection of the complexes in tissue from patients suspected of mitochondrial disease. Emphasis lies on the diagnostic potential of these techniques to differentiate mtDNA from nuclear mutations. This e-book — a curated collection from eLS, WIREs, and Current Protocols — offers a fantastic introduction to the field of mitochondrial diseases for students or interdisciplinary collaborators. Table of Contents: Introduction Mitochondrial DNA Copy Number Alterations in Human Cancers eLS Man Yu Mitochondrial Disorders: Nuclear Gene Mutations eLS Daniele Ghezzi and Massimo Zeviani Mitochondria as a Key Determinant of Aging eLS Ludivine Walter and Siu Sylvia Lee Advanced Reviews Mitochondrial tRNA Mutations and Disease WIREs RNA John W. Yarham, Joanna L. Elson, Emma L. Blakely, Robert McFarland, Robert W. Taylor Human Mitochondrial Diseases Caused by Lack of Taurine Modification in Mitochondrial tRNAs WIREs RNA Suzuki Tsutomu, Nagao Asuteka, Suzuki Takeo Protocols Next Generation Sequencing to Characterize Mitochondrial Genomic DNA Heteroplasmy Current Protocols in Human Genetics Taosheng Huang Histochemical Methods for the Diagnosis of Mitochondrial Diseases Current Protocols in Human

Genetics Boel De Paepe, Jan L. De Bleecker, Rudy Van Coster

David Reich describes how the revolution in the ability to sequence ancient DNA has changed our understanding of the deep human past. This book tells the emerging story of our often surprising ancestry - the extraordinary ancient migrations and mixtures of populations that have made us who we are.

Nearly thirty million species of organisms are believed to now live on Earth. In addition to accumulating evidence from classical biology, paleontology and earth science, the recent progress of molecular biology has provided new insights into understanding how present-day organisms have evolved with such tremendous diversity. Molecular biological studies show us that all living forms, including E. coli and human beings, derive from a single ancestor that emerged some 4 billion years ago on Earth. This volume aims to discuss the motifs of organismic evolution from the viewpoints of biogeo-interactions and diversification of the genetic systems. Based on these fundamental understandings, the last section of this volume is devoted to human evolution that includes phylogeny of man as well as evolution of human culture. Such comprehensive discussion will give us a synthesized view of the evolution of life, that is undoubtedly one of the most important problems not only for science but also for human culture in general.

Describes how a scientist linked the DNA found in a five-thousand-year-old man to modern-day relatives and explains how all modern individuals can trace their genetic

makeup back to prehistoric times to seven primeval women.

The human mitochondrial DNA (mtDNA) genome must be faithfully maintained by the mitochondrial DNA replication machinery. Deficiencies in mtDNA maintenance result in the accumulation of mutations and deletions, which have been associated with a number of neuromuscular degenerative disorders including, mtDNA depletion syndrome, Alpers syndrome, progressive external opthalmoplegia (PEO), and sensory ataxic neuropathy, dysarthria, and opthalmoparesis (SANDO). The mtDNA replication machinery is comprised of a nuclearly-encoded DNA polymerase gamma (Pol [gamma]), single-stranded DNA binding protein (mtSSB), and a hexameric mtDNA helicase. In this work, we employed quantitative pre-steady state kinetic techniques to establish the mechanisms responsible for the replication of the human mitochondrial DNA by Pol [gamma] and explored the effects of point mutations that are observed in heritable diseases. With our biochemical characterization of mutants of Pol [gamma], we have shown unique characteristics that would lead to profound physiological consequences over time. Additionally, we have made significant progress towards reconstitution of the mitochondrial DNA replisome by monitoring DNA polymerization that is dependent on helicase unwinding of double stranded DNA. Overall, this work provides a better understanding of the mechanism of mtDNA replication and has important implications toward understanding the role of mitochondrial DNA replication in mitochondrial disease, ageing and cancer. In addition to the work on the mtDNA replisome, we have applied pre-steady state kinetic techniques to better understand the mechanism of RNA-dependent DNA polymerization by HIV reverse transcriptase (HIV-RT). This enzyme is responsible for the replication of the viral genome in HIV and is a common target for anti-HIV drugs. We have characterized the role

of enzyme conformational changes in the kinetics of incorporation of correct nucleotide and the Nucleotide Reverse Transcriptase Inhibitor (NRTI) AZT by wild-type enzyme, as well as a mutant with clinical resistance to AZT. This work provides a better understanding of the complete mechanism of RNA-dependent DNA polymerization, the changes in the mechanism in the presence of inhibitor and the development of resistance to this nucleoside analog; and thereby this work contributes to the long-term goal of designing more effective drugs that can possibly deter resistance and be used successfully for treatment of HIV.

Mitochondrial dysfunction is increasingly being recognized as the basis of a wide variety of human diseases. Providing an authoritative update on our current knowledge of mitochondrial medicine, this text draws together world authorities from various fields to present general therapeutic strategies, as well as the treatments presently available in different specialties - thus making it essential reading for clinicians involved with the management of patients with mitochondrial diseases. A unique work, this text covers a range of specialties, including cardiology, ophthalmology, otology, nephrology, gastroenterology, hematology-oncology, and reproductive medicine, and does not focus exclusively on the more commonly known neurologic conditions. An accessible, user-friendly text, it also presents translational concepts of mitochondrial biogenesis and genetics in vignettes related to specific questions raised by the disease under discussion, rather than concentrating on basic science, which can often intimidate clinicians. This pioneering work is primarily directed to a clinical audience who are interested in the diverse and diagnostically challenging clinical presentations of mitochondrial diseases and their pathophysiology.

The very short genomes of mitochondria summarize the complexity of molecular biology and

its interactions with cellular and whole organism biology. Studies of mitogenomes contribute to the understanding of molecular biology and evolution, and to health management. Despite or even due to their small sizes, mitogenomes continue to surprise us. Studies of mitogenomes reveal the details of molecular organization and its evolution under constraints for miniaturization.

The Human Mitochondrial Genome: From Basic Biology to Disease offers a comprehensive, up-to-date examination of human mitochondrial genomics, connecting basic research to translational medicine across a range of disease types. Here, international experts discuss the essential biology of human mitochondrial DNA (mtDNA), including its maintenance, repair, segregation, and heredity. Furthermore, mtDNA evolution and exploitation, mutations, methods, and models for functional studies of mtDNA are dealt with. Disease discussion is accompanied by approaches for treatment strategies, with disease areas discussed including cancer, neurodegenerative, age-related, mtDNA depletion, deletion, and point mutation diseases. Nucleosides supplementation, mitoTALENs, and mitoZNF nucleases are among the therapeutic approaches examined in-depth. With increasing funding for mtDNA studies, many clinicians and clinician scientists are turning their attention to mtDNA disease association. This book provides the tools and background knowledge required to perform new, impactful research in this exciting space, from distinguishing a haplogroup-defining variant or disease-related mutation to exploring emerging

therapeutic pathways. Fully examines recent advances and technological innovations in the field, enabling new mtDNA studies, variant and mutation identification, pathogenic assessment, and therapies Disease discussion accompanied by diagnostic and therapeutic strategies currently implemented clinically Outlines and discusses essential research protocols and perspectives for young scientists to pick up Features an international team of authoritative contributors from basic biologists to clinician-scientists

Mutations within mitochondrial DNA (mtDNA) and the nuclear genes involved in the maintenance of mitochondrial DNA have been linked to a wide range of human diseases, including several of the most common diseases of aging. In Mitochondrial DNA: Methods and Protocols internationally recognized authorities describe in great detail the methods they have perfected to analyze mtDNA and the proteins involved in its maintenance. The analytical techniques cover the purification of mtDNA from a variety of sources and the analysis of DNA for both deletions, point mutations, and damage, for replication intermediates, and for following the fate of mtDNA outside of the mitochondria. Additional analytical methods are presented for analyzing the proteins and enzymes that maintain mtDNA. Each readily reproducible protocol includes step-by-step instructions, tips on avoiding pitfalls and extending the method to other situation, and introductory material explaining the theory behind the process. Comprehensive and timely, Mitochondrial DNA: Methods and Protocols offers both basic and clinical

researchers proven cutting-edge methods for analyzing the role mtDNA plays in the aging process, apoptosis, and possibly some cancers, and for investigating the cause of mitochondrial dysfunction and disease.

Human mitochondrial DNA is a distinct, compact genetic system that encodes proteins crucial for energy metabolism in the cell. Due to its reduced size and relatively simple organisation, all the regulatory factors directing the expression of the mitochondrial genome are encoded by nuclear DNA. It is evident that mitochondrial gene expression is regulated at different levels, which is reflected by the numerous diseases associated with mutations in both nuclear and mitochondrial DNA-encoded mitochondrial proteins. Research focusing on the identification and characterisation of RNA-binding proteins as regulators of mitochondrial function is ongoing. However, the components and mechanisms involved in the post-transcriptional regulation of mitochondrial DNA are not well understood. The aim of this research project was to investigate different aspects of the regulation of human mitochondrial gene expression via the direct action of nuclear-encoded mitochondrial proteins on RNA metabolism. First, I validated the proteins responsible for 5' end processing of mitochondrial precursor transcripts and identified the protein responsible for 3' end processing cleavage, showing that they are important for mitochondrial function. Next, I studied a previously uncharacterised mitochondrial ribosomal subunit protein and found that it is an important factor in the regulation of protein synthesis. Finally, I examined a protein that has multiple and independent

functions in the organelle and identified it as a new target for the estrogenic modulation of mitochondrial gene expression via the estrogen receptor alpha. Both the nuclear and the mitochondrial genomes contribute to the mitochondrial proteome and hence to mitochondrial function. Because mitochondria possess a genome that is central to multiple cellular functions, understanding the different levels and mechanisms involved in the regulation of mitochondrial gene expression is essential in elucidating the contribution of mitochondrial dysfunction to human disease.

This volume investigates how the mitochondrial genome is transmitted, segregated, and inherited. It starts by describing mtDNA mutations and deletions and how these impact on the offspring's well-being. It progresses to discuss how mutations to the mtDNA-nuclear-encoded transcription, replication and translational factors lead to mtDNA-depletion syndromes and how these affect cellular function and lead to the pathology of human mitochondrial disease. It also highlights the importance of the mitochondrial assembly factors and how mutations to these can lead to mitochondrial disease. The reader is then introduced to how mtDNA is transmitted through the oocyte and how stem cells can be used to study mitochondrial biogenesis and mtDNA replication and transcription in undifferentiated pluripotent and differentiating cells and how mitochondria adapt during this process. It then discusses how diseases like

cancer are initiated and regulated by mutations to mitochondrial DNA and dysfunctional mitochondria. Finally, it draws on assisted reproductive technologies to discuss how some of these approaches might be adapted to prevent the transmission of mutant and deleted mtDNA from one generation to the next.

Mitochondrial DNA is one of the most closely explored genetic systems, because it can tell us so much about the human past. This book takes a unique perspective, presenting the disparate strands that must be tied together to exploit this system. From molecular biology to anthropology, statistics to ancient DNA, this first volume of three presents a comprehensive global picture and a critical appraisal of human mitochondrial DNA variation.