DOWNLOAD PDF GENOME INTEGRITY (GENOME DYNAMICS AND STABILITY)

Chapter 1 : - Genome Integrity (Genome Dynamics and Stability) by Dirk-Henner Lankenau

Cells and viruses keep a genome able to multiplication, variation and heredity. A genome consists of chromosomes, every being constructed up of two complementary strands of nucleic acid referred to as DNA.

In humans, mutations that would change an amino acid within the protein coding region of the genome occur at an average of only 0. In other cases, there are structural alterations chromosomal translocations , deletions In these cases, it is indicated that the affected organism presents genome instability also genetic instability, or even chromosomic instability. The process of genome instability often leads to a situation of aneuploidy , in which the cells present a chromosomic number that is either higher or lower than the normal complement for the species. The replisome must be able to navigate obstacles such as tightly wound chromatin with bound proteins, single and double stranded breaks which can lead to the stalling of the replication fork. Each protein or enzyme in the replisome must perform its function well to result in a perfect copy of DNA. Mutations of proteins such as DNA polymerase, ligase, can lead to impairment of replication and lead to spontaneous chromosomal exchanges. Mutations in Tel1, Mec1, and Rmr3 helicase result in a significant increase of chromosomal recombination. ATR responds specifically to stalled replication forks and single-stranded breaks resulting from UV damage while ATM responds directly to double-stranded breaks. These proteins also prevent progression into mitosis by inhibiting the firing of late replication origins until the DNA breaks are fixed by phosphorylating CHK1, CHK2 which results in a signaling cascade arresting the cell in S-phase. These sites are called fragile sites, and can occur commonly as naturally present in most mammalian genomes or occur rarely as a result of mutations, such as DNA-repeat expansion. These trinucleotide repeats can form into hairpins, leading to difficulty of replication. Under replication stress, such as defective machinery or further DNA damage, DNA breaks and gaps can form at these fragile sites. Transcription-associated instability[edit] In both E. The coding or non-transcribed strand accumulates more mutations than the template strand. This is due to the fact that the coding strand is single-stranded during transcription, which is chemically more unstable than double-stranded DNA. During elongation of transcription, supercoiling can occur behind an elongating RNA polymerase, leading to single-stranded breaks. When the coding strand is single-stranded, it can also hybridize with itself, creating DNA secondary structures that can compromise replication. This suggests that transcription is an obstacle to replication, which can lead to increased stress in the chromatin spanning the short distance between the unwound replication fork and transcription start site, potentially causing single-stranded DNA breaks. One such locale is the Ig genes. In a pre-B cell, the region consists of all V, D, and J segments. Uracil normally does not exist in DNA, and thus the base is excised and the nick is converted into a double-stranded break which is repaired by non-homologous end joining NHEJ. This procedure is very error-prone and leads to somatic hypermutation. This genomic instability is crucial in ensuring mammalian survival against infection. V, D, J recombination can ensure millions of unique B-cell receptors; however, random repair by NHEJ introduces variation which can create a receptor that can bind with higher affinity to antigens. Overall, it seems that oxidative stress is a major cause of genomic instability in the brain. A particular neurological disease arises when a pathway that normally prevents oxidative stress is deficient, or a DNA repair pathway that normally repairs damage caused by oxidative stress is deficient. In cancer[edit] In cancer , genome instability can occur prior to or as a consequence of transformation. Situations of genome instability as well as aneuploidy are common in cancer cells, and they are considered a "hallmark" for these cells. The unpredictable nature of these events are also a main contributor to the heterogeneity observed among tumour cells. It is currently accepted that sporadic tumors non-familial ones are originated due to the accumulation of several genetic errors. Losing genetic stability will favour tumor development, because it favours the generation of mutants that can be selected by the environment. In the entire genome including non-protein coding regions there are only about 70 new mutations per generation in humans. Externally and endogenously caused damages may be converted into mutations by inaccurate

translesion synthesis or inaccurate DNA repair e. Very frequent mutations in cancer[edit] As noted above, about 3 or 4 driver mutations and 60 passenger mutations occur in the exome protein coding region of a cancer. The average number of DNA sequence mutations in the entire genome of a breast cancer tissue sample is about 20, Mutation rates substantially increase sometimes by fold in cells defective in DNA mismatch repair [32] [33] or in homologous recombinational DNA repair. In addition, faulty repair of these accumulated DNA damages may give rise to epigenetic alterations or epimutations. Such cells, with both proliferative advantages and one or more DNA repair defects causing a very high mutation rate , likely give rise to the 20, to 80, total genome mutations frequently seen in cancers. DNA repair deficiency in cancer[edit] In somatic cells, deficiencies in DNA repair sometimes arise by mutations in DNA repair genes, but much more often are due to epigenetic reductions in expression of DNA repair genes. Lymphomas as a consequence of genome instability[edit] Cancers usually result from disruption of a tumor repressor or dysregulation of an oncogene. Knowing that B-cells experience DNA breaks through development can give insight to the genome of lymphomas. Many types of lymphoma are caused by chromosomal translocation, which can arise from breaks in DNA leading to incorrect joining. Since immunoglobulins are essential to a lymphocyte and highly expressed to increase detection of antigens, c-myc is then also highly expressed leading to transcription of its targets which are involved in cell proliferation. Mantle cell lymphoma is characterized by fusion of cyclin D1 to the immunoglobulin locus. Cyclin D1 inhibits Rb, a tumor suppressor, leading to tumorigenesis. Follicular lymphoma results from the translocation of immunoglobulin promoter to the Bcl-2 gene, giving rise to large amounts of Bcl-2 protein which inhibits apoptosis. DNA-damaged B-cells no longer undergo apoptosis leading to further mutations which could affect driver genes leading to tumorigenesis. Ann N Y Acad Sci. Basic Clin Pharmacol Toxicol. Isolation and genetic characterization of hyper-recombination mutations". Annual Review of Genetics. DNA repair defects and neurological disease. Nat Clin Pract Neurol. April , "Cancer-susceptibility genes. Gatekeepers and caretakers", Nature, PLoS Genet ;4 8 e Genetical and clinical observations in the first twenty-seven patients". Am J Hum Genet.

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Chapter 2 : Genome instability - Wikipedia

The Springer series "Genome Dynamics and Stability" encompasses intriguing key aspects of the biology, biochemistry, and molecular biology of the integrity and dynamics of genomes. While not excluding prokaryotes, it focuses on eukaryotes and metazoans, whose genomes are structured by a patchwork of.

The author responsible for distribution of materials integral to the findings presented in this article in accordance with the policy described in the Instructions for Authors www. Received Oct 5; Accepted Oct This article has been cited by other articles in PMC. Abstract The chloroplast cp genome is organized as nucleoids that are dispersed throughout the cp stroma. Previously, a cp homolog of bacterial recombinase RecA cpRECA was shown to be involved in the maintenance of cp genome integrity by repairing damaged chloroplast DNA and by suppressing aberrant recombination between short dispersed repeats in the moss Physcomitrella patens. Here, overexpression and knockdown analysis of cpRECA in the green alga Chlamydomonas reinhardtii revealed that cpRECA was involved in cp nucleoid dynamics as well as having a role in maintaining cp genome integrity. Overexpression of cpRECA tagged with yellow fluorescent protein or hemagglutinin resulted in the formation of giant filamentous structures that colocalized exclusively to chloroplast DNA and cpRECA localized to cp nucleoids in a heterogenous manner. Knockdown of cpRECA led to a significant reduction in cp nucleoid number that was accompanied by nucleoid enlargement. This phenotype resembled those of gyrase inhibitor-treated cells and monokaryotic chloroplast mutant cells and suggested that cpRECA was involved in organizing cp nucleoid dynamics. The cp genome also was destabilized by induced recombination between short dispersed repeats in cpRECA-knockdown cells and gyrase inhibitor-treated cells. Taken together, these results suggest that cpRECA and gyrase are both involved in nucleoid dynamics and the maintenance of genome integrity and that the mechanisms underlying these processes may be intimately related in C. Chloroplasts cp s are plant organelles that are responsible for photosynthesis and the supply of certain metabolites. As a result, cpDNA genomes are now small generally â€” kb in size compared with the genomes of ancestrally related cyanobacteria. The remaining cpDNA is densely packed and encodes genes essential for cp function and photosynthesis Bungard, ; Green, In most plants, cpDNA is composed of four regions: The cp s usually possess 10 to copies of the genomic DNA, some of which are organized into a nucleoid similar to that formed by bacterial chromosomal DNA Kuroiwa, The nucleoid is thereby involved in the regulation of DNA replication and transcription Powikrowska et al. The cp nucleoids are found as small particles dispersed throughout the cp stroma in a diverse range of plant and algal taxa. However, the shape and distribution of cp nucleoids change dynamically according to cell cycle phase Ehara et al. However, the mechanisms governing the dynamic micromorphology of cp nucleoids remain largely unknown. A few studies examined mutants defective in cp nucleoid segregation. The monokaryotic chloroplast moc mutants exhibiting impaired cp nucleoid dispersion were obtained by insertional mutagenesis in Chlamydomonas reinhardtii Misumi et al. The moc mutants contained a single large cp nucleoid that was comparable in size to the nucleus, but the overall amount of cpDNA was slightly lower than in wild-type cells. The mutants exhibited aberrant cp nucleoid segregation, which resulted in cells with lower amounts of cpDNA. The gene responsible for moc phenotypes remains unidentified. These studies indicate that there may be links between cp nucleoid micromorphology and cpDNA molecular structure that are related to cpDNA replication. Distinct mechanisms maintain cpDNA integrity in plants that differ from the mechanisms underlying the establishment and maintenance of micromorphological cpDNA structure. Homologous recombination HR repair is a fundamental pathway that is critical in the recombination, replication, and repair of DNA defects such as double-strand breaks DSB s and stalled replication forks, thereby maintaining genome stability. RAD51 is a eukaryotic homolog Shinohara et al. Active HR occurs between large cp inverted repeats Kolodner and Tewari, , and RecA-related strand transfer activity is observed in cp extracts Cerutti et al. Expression of an Escherichia coli dominant-negative RecA protein in C. Some mutant studies examined the

role of cpRECA in the maintenance of cp genome integrity. In addition, recombination between short dispersed repeats SDR s; less than bp in cpDNA was higher in knockout mutants than in the wild type Odahara et al. This suggests that cpRECA may suppress aberrant recombination between SDR s in cp and play a similar role in maintaining cp genome stability to that of mitochondrial RECA in mitochondrial genome stability Odahara et al. After reproduction for several generations, Arabidopsis cpRECA mutants exhibited variegation in leaves and enhanced sensitivity to DSB - and reactive oxygen species-inducing agents Rowan et al. Recent next-generation sequencing approaches have revealed that Arabidopsis cpRECA acts to suppress U-turn like rearrangements mediated by microhomology Zampini et al. In land plants, cp nucleoid morphology and molecular structure are complex and vary considerably depending on tissue type, developmental stage, age, and environment Oldenburg and Bendich, Furthermore, as plant cells contain multiple cp s that actively move around in response to environmental and other cues Wada, , monitoring the micromorphology of cp nucleoids at high resolution can be problematic Terasawa and Sato, Therefore, we used the unicellular green alga Chlamydomonas reinhardtii as a simple model system. In this research, we performed detailed functional analysis of cpRECA, with special focus on its impact on cp nucleoid dynamics and cp genome stability. We also analyzed the effect of gyrase inhibition on cp nucleoid dynamics and cp genome stability. The results demonstrate that cpRECA and gyrase are both involved in cp nucleoid dynamics and cp genome stability. Immunofluorescence microscopy using an antibody raised against C. S1 confirmed that C.

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Chapter 3 : Genome Integrity: 1 (Genome Dynamics and Stability) - Ebook pdf and epub

Cells and viruses maintain a genome capable of multiplication, variation and heredity. A genome consists of chromosomes, each being built up of two complementary strands of nucleic acid known as DNA.

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Chapter 4 : Chromatin and the genome integrity network

Preface Genome dynamics and stability are the non plus ultra requirements for cellu- lar life. No matter whether life began with metabolism, with self-replicating genetic molecules, or as a cooperative chemical phenomenon, all cells and.

Development and application of DNA molecular markers with emphasis on transposable elements for the assessment of the natural and induced genetic diversity. Population genetics, micro-evolutionary changes and ecology. Genetic bases of abiotic stress. Epigenetic mechanisms of programming and reprogramming of the genome in eukaryotic organisms; Mechanisms of regulation of imprinted genes; Epigenetic changes in mouse parthenogenesis. Ivelina Nikolova, Research Scientist E-mail: Plant Genetics; DNA damages, DNA repair, Mutations; Molecular cytogenetic characterization of plants, DNA markers and fluorescent in situ hybridization of genomic DNA; DNA sequencing, microchips; Biotic and abiotic stress factors radiation ; Positional-specific effects in the chromosomes of barley, chromosome rearrangements, reconstructed barley karyotypes; Statistical methods of analysis of the data. Ilija Nikolov, Research Scientist Phone: Genetic and epigenetic mechanisms in carcinogenesis in humans; DNA markers. Zlatina Gospodinova, Research Scientist E-mail: Genetic and epigenetic mechanisms in humans carcinogenesis; Balkan Endemic Nephropathy; Breast Cancer; Antitumor potential of Bulgarian medicinal plants. Georgi Antov, Research Scientist E-mail: Journal of Molecular Evolution 84 Turkish Journal of Botany 39 6 Karyotype reconstruction modulates the sensitivity of barley genome to radiation-induced DNA and chromosomal damage. Molecular cytogenetic characterization of a new reconstructed barley karyotype. Dimitrova A, Stoilov L. Molecular variability in barley structural mutants produced by gamma-irradiation. Plant Mutation Reports, p. Karov R, Kovacevik B. Morphological and molecular characterization of colletotrichum coccodes isolated from pepper cultivated in Bulgaria and Macedonia. Bonchev G, Parisod C. Breast cancer patients with hypermethylation in the promoter of BRCA1 gene exhibit favorable clinical status. Neoplasma 59, doi: Chek2 gene alterations independently increase the risk of death from breast cancer in Bulgarian patients. Journal of Applied Genetics, 53, Processing of DNA double strand br eaks by alternative non-homologous end-joining in hyperacetylated chromatin Genome Integrity 3: Current Trends in Plant Protection, Belgrade, Mijatovic Unusual Colletotrichum Sp. Molecular cytogenetic characterization of two high protein wheat-Thinopyrum intermedium partial amphiploids. Journal of Applied Genetics, Bonchev G, Pearce S, Georgiev S Retrotransposons and ethyle methanesulphonate induced genetic diversity in sphaerococcum mutant forms of hexaploid wheat and Triticale. J Cancer Res Clin Oncol. Penkov LI, Platonov ES Modulation the effects of genomic imprinting by 5-methyldeoxycytidin in parthenogenetic mouse embryos developed in vitro and in vivo. Induced Plant Mutations in the Genomics Era. Genetics and Breeding, Kitanova Genetic analysis of sphaerococcum mutant forms of hexaploid wheats and triticale MT47, Biotechnol. Georgieva M, Stoilov L. Assessment of DNA strand breaks induced by bleomycin in barley by the comet assay. Environmental and Molecular Mutagenesis, Adaptive response to DNA and chromosomal damage induced by X-rays in human blood lymhocytes. Mutagenesis, 22 2 , , Manova V. Mutation Research, , pp.

Chapter 5 : Genome dynamics and stability : Institute of Plant Physiology and Genetics â€“ BAS

Molecular mechanisms of DNA repair and genome stability in higher plants. Chromosome and DNA markers for genome identification and assessment of mutant and natural genetic diversity in plants. Molecular mechanisms of eukaryotic carcinogenesis and genome imprinting.

Chapter 6 : Dynamic Interplay between Nucleoid Segregation and Genome Integrity in Chlamydomonas Cl

The maintenance of genome integrity is essential for organism survival and for the inheritance of traits to offspring.

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Genomic instability is caused by DNA damage, aberrant DNA replication or uncoordinated cell division, which can lead to chromosomal aberrations and gene mutations. Recently.