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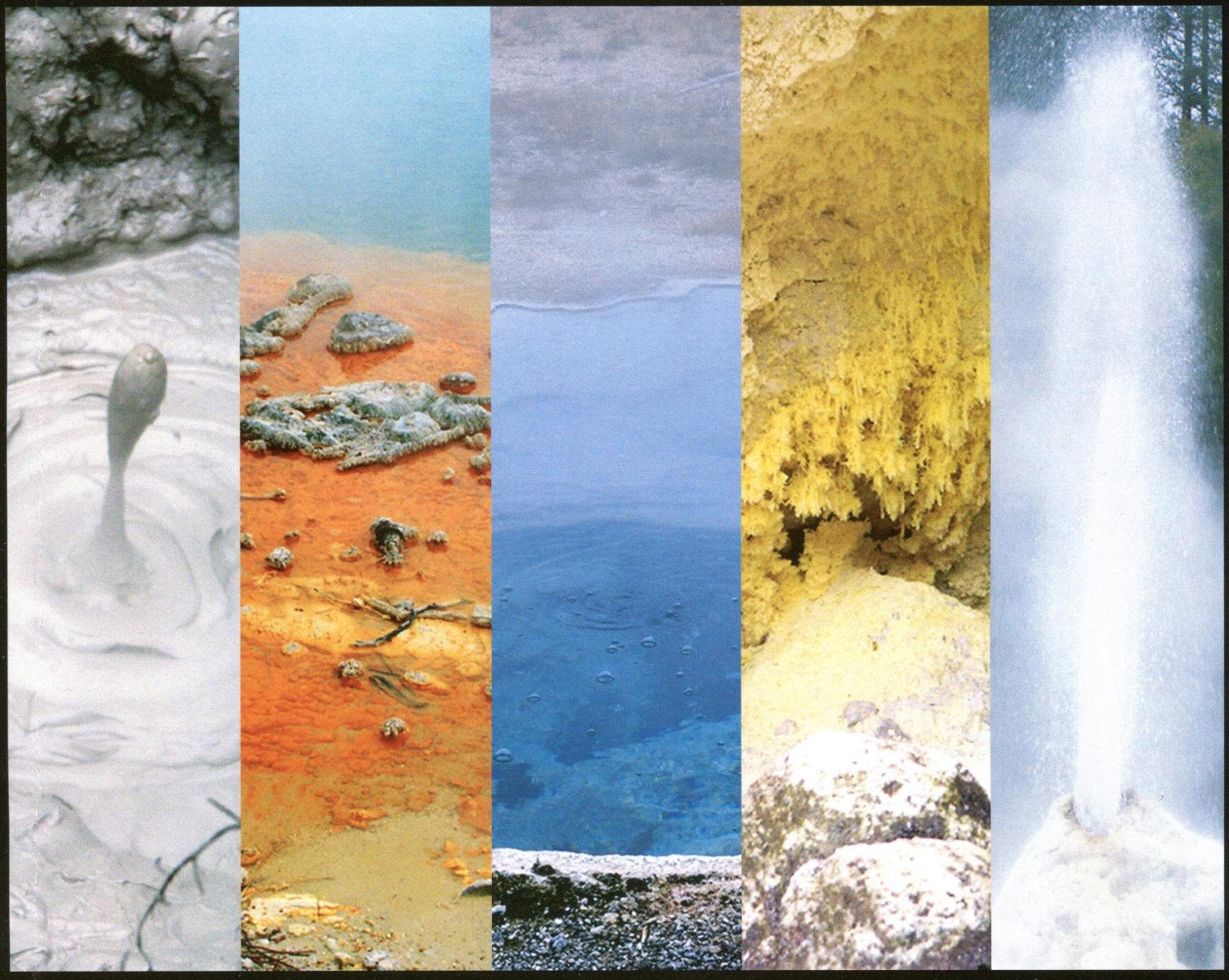
MICROBIOLOGY AND MOLECULAR BIOLOGY REVIEWS



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CONTENTS/SUMMARIES

REVIEWS

Summary: Bacterial genomes are remarkably stable from one generation to the next but are plastic on an evolutionary time scale, substantially shaped by horizontal gene transfer, genome rearrangement, and the activities of mobile DNA elements. This implies the existence of a delicate balance between the maintenance of genome stability and the tolerance of genome instability. In this review, we describe the specialized genetic elements and the endogenous processes that contribute to genome instability. We then discuss the consequences of genome instability at the physiological level, where cells have harnessed instability to mediate phase and antigenic variation, and at the evolutionary level, where horizontal gene transfer has played an important role. Indeed, this ability to share DNA sequences has played a major part in the evolution of life on Earth. The evolutionary plasticity of bacterial genomes, coupled with the vast numbers of bacteria on the planet, substantially limits our ability to control disease.

Summary: All living organisms are continuously faced with endogenous or exogenous stress conditions affecting genome stability. DNA repair pathways act as a defense mechanism, which is essential to maintain DNA integrity. There is much to learn about the regulation and functions of these mechanisms, not only in human cells but also equally in divergent organisms. In trypanosomatids, DNA repair pathways protect the genome against mutations but also act as an adaptive mechanism to promote drug resistance. In this review, we scrutinize the molecular mechanisms and DNA repair pathways which are conserved in trypanosomatids. The recent advances made by the genome consortiums reveal the complete genomic sequences of several pathogens. Therefore, using bioinformatics and genomic sequences, we analyze the conservation of DNA repair proteins and their key protein motifs in trypanosomatids. We thus present a comprehensive view of DNA repair processes in trypanosomatids at the crossroads of DNA repair and drug resistance.

Summary: Clustered regularly interspaced short palindromic repeats (CRISPR) and CRISPR-associated (Cas) genes are present in many bacterial and archaeal genomes. Since the discovery of the typical CRISPR loci in the 1980s, well before their physiological role was revealed, their variable sequences have been used as a complementary typing tool in diagnostic, epidemiologic, and evolutionary analyses of prokaryotic strains. The discovery that CRISPR spacers are often identical to sequence fragments of mobile genetic elements was a major breakthrough that eventually led to the elucidation of CRISPR-Cas as an adaptive immunity system. Key elements of this unique prokaryotic defense system are small CRISPR RNAs that guide nucleases to complementary target nucleic acids of invading viruses and plasmids, generally followed by the degradation of the invader. In addition, several recent studies have pointed at direct links of CRISPR-Cas to regulation of a range of stress-related phenomena. An interesting example concerns a pathogenic bacterium that possesses a CRISPR-associated ribonucleoprotein complex that may play a dual role in defense and/or virulence. In this review, we describe recently reported cases of potential involvement of CRISPR-Cas systems in bacterial stress responses in general and bacterial virulence in particular.

Summary: The metabolism of *Archaea*, the third domain of life, resembles in its complexity those of *Bacteria* and lower *Eukarya*. However, this metabolic complexity in *Archaea* is accompanied by the absence of many "classical" pathways, particularly in central carbohydrate metabolism. Instead, *Archaea* are characterized by the presence of unique, modified variants of classical pathways such as the Embden-Meyerhof-Parnas (EMP) pathway and the Entner-Doudoroff (ED)

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pathway. The pentose phosphate pathway is only partly present (if at all), and pentose degradation also significantly differs from that known for bacterial model organisms. These modifications are accompanied by the invention of "new," unusual enzymes which cause fundamental consequences for the underlying regulatory principles, and classical allosteric regulation sites well established in *Bacteria* and *Eukarya* are lost. The aim of this review is to present the current understanding of central carbohydrate metabolic pathways and their regulation in *Archaea*. In order to give an overview of their complexity, pathway modifications are discussed with respect to unusual archaeal biocatalysts, their structural and mechanistic characteristics, and their regulatory properties in comparison to their classic counterparts from *Bacteria* and *Eukarya*. Furthermore, an overview focusing on hexose metabolic, i.e., glycolytic as well as gluconeogenic, pathways identified in archaeal model organisms is given. Their energy gain is discussed, and new insights into different levels of regulation that have been observed so far, including the transcript and protein levels (e.g., gene regulation, known transcription regulators, and posttranslational modification via reversible protein phosphorylation), are presented.

Summary: After several decades of use of glyphosate, the active ingredient in weed killers such as Roundup, in fields, forests, and gardens, the biochemical pathway of transformation of glyphosate phosphorus to a useful phosphorus source for microorganisms has been disclosed. Glyphosate is a member of a large group of chemicals, phosphonic acids or phosphonates, which are characterized by a carbon-phosphorus bond. This is in contrast to the general phosphorus compounds utilized and metabolized by microorganisms. Here phosphorus is found as phosphoric acid or phosphate ion, phosphoric acid esters, or phosphoric acid anhydrides. The latter compounds contain phosphorus that is bound only to oxygen. Hydrolytic, oxidative, and radical-based mechanisms for carbon-phosphorus bond cleavage have been described. This review deals with the radical-based mechanism employed by the carbon-phosphorus lyase of the carbon-phosphorus lyase pathway, which involves reactions for activation of phosphonate, carbon-phosphorus bond cleavage, and further chemical transformation before a useful phosphate ion is generated in a series of seven or eight enzyme-catalyzed reactions. The *phn* genes, encoding the enzymes for this pathway, are widespread among bacterial species. The processes are described with emphasis on glyphosate as a substrate. Additionally, the catabolism of glyphosate is intimately connected with that of aminomethylphosphonate, which is also treated in this review. Results of physiological and genetic analyses are combined with those of bioinformatics analyses.

Cover photograph (Copyright © 2014, American Society for Microbiology. All Rights Reserved): Geothermal areas and hot springs from Waiotapu geothermal area (Roturua, New Zealand) and Yellowstone National Park (United States). (Leftmost) A mud pool in the Waiotapu geothermal area, Roturua, New Zealand (courtesy of Ian Haidl [Microbiology and Immunology, Dalhousie University, Halifax, Nova Scotia, Canada]). (Second from left) Champagne Pool in the Waiotapu geothermal area, Roturua, New Zealand (courtesy of Ian Haidl). (Center) A hot spring in Yellowstone National Park, United States (courtesy of Sonja-Verena Albers [Molecular Biology of Archaea, Max-Planck-Institute for Terrestrial Microbiology, Marburg, Germany]). (Second from right) Sulfur deposits in the Waiotapu geothermal area, Roturua, New Zealand (courtesy of Ian Haidl). (Rightmost) Lady Knox Geyser, Waiotapu geothermal area, Roturua, New Zealand (courtesy of Ian Haidl). Design by Bettina Siebers (Molecular Enzyme Technology and Biochemistry, University of Duisburg-Essen, Germany) and Monika Helak (style & print, Essen, Germany). *(See related article on page 89.)*