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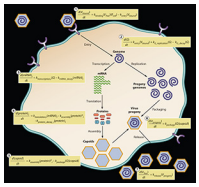
COVER IMAGE



Cover photograph: When a virus infects a cell, how much time will elapse before viral progeny are released, and how many viral progeny particles will the process yield? To address these questions, one may mathematically account for the mechanisms, rates, and resources of the diverse biochemical and biophysical processes that define the interaction of a virus with its host cell. (*See related article in June 2018, vol. 82, no. 2, e00066-17.*)

REVIEWS

Summary: The literature review presented here details recent research involving members of the poly(ADP-ribose) polymerase (PARP) family of proteins. Among the 17 recognized members of the family, the human enzyme PARP1 is the most extensively studied, resulting in a number of known biological and metabolic roles. This review is focused on the roles played by PARP enzymes in host-pathogen interactions and in diseases with an associated inflammatory response. In mammalian cells, several PARPs have specific roles in the antiviral response; this is perhaps best illustrated by PARP13, also termed the zinc finger antiviral protein (ZAP). Plant stress responses and immunity are also regulated by poly(ADP-ribosyl)ation. PARPs promote inflammatory responses by stimulating proinflammatory signal transduction pathways that lead to the expression of cytokines and cell adhesion molecules. Hence, PARP inhibitors show promise in the treatment of inflammatory disorders and conditions with an inflammatory component, such as diabetes, arthritis, and stroke. These functions are correlated with the biophysical characteristics of PARP family enzymes. This work is important in providing a comprehensive understanding of the molecular basis of pathogenesis and host responses, as well as in the identification of inhibitors. This is important because the identification of inhibitors has been shown to be effective in arresting the progression of disease.

Summary: Species within the genus *Burkholderia* exhibit remarkable phenotypic diversity. Genomic plasticity, including genome reduction and horizontal gene transfer, has been correlated with virulence traits in several species. However, the conservation of virulence genes in species otherwise considered to have limited potential for infection suggests that phenotypic diversity may not be explained solely on the basis of genetic diversity. Instead, differential organization and control of gene regulatory networks may underlie many phenotypic differences. In this review, we evaluate how regulation of gene expression by members of the multiple antibiotic resistance regulator (MarR) family of transcription factors may contribute to shaping the physiological diversity of *Burkholderia* species, with a focus on the clinically relevant human pathogens. All *Burkholderia* species encode a relatively large number of MarR proteins, a feature common to bacteria that must respond to environmental changes such as those associated with host invasion. However, evolution of gene regulatory

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networks has likely resulted in orthologous transcription factors controlling disparate sets of genes. Adaptation to, and survival in, diverse habitats, including a human or plant host, is key to the success of *Burkholderia* species as (opportunistic) pathogens, and recent reports suggest that control of virulence-associated genes by MarR proteins features prominently among the survival strategies employed by these species. We suggest that identification of MarR regulons will contribute significantly to clarification of virulence determinants and phenotypic diversity.

Summary: Ribosyl 1,5-bisphosphate (PRibP) was discovered 65 years ago and was believed to be an important intermediate in ribonucleotide metabolism, a role immediately taken over by its "big brother" phosphoribosyldiphosphate. Only recently has PRibP come back into focus as an important player in the metabolism of ribonucleotides with the discovery of the pentose bisphosphate pathway that comprises, among others, the intermediates PRibP and ribulose 1,5-bisphosphate (cf. ribose 5-phosphate and ribulose 5-phosphate of the pentose phosphate pathway). Enzymes of several pathways produce and utilize PRibP not only in ribonucleotide metabolism but also in the catabolism of phosphonates, i.e., compounds containing a carbon-phosphorus bond. Pathways for PRibP metabolism are found in all three domains of life, most prominently among organisms of the archaeal domain, where they have been identified either experimentally or by bioinformatic analysis within all of the four main taxonomic groups, *Euryarchaeota*, TACK, DPANN, and Asgard. Advances in molecular genetics of archaea have greatly improved the understanding of the physiology of PRibP metabolism, and reconciliation of molecular enzymology and three-dimensional structure analysis of enzymes producing or utilizing PRibP emphasize the versatility of the compound. Finally, PRibP is also an effector of several metabolic activities in many organisms, including higher organisms such as mammals. In the present review, we describe all aspects of PRibP metabolism, with emphasis on the biochemical, genetic, and physiological aspects of the enzymes that produce or utilize PRibP. The inclusion of high-resolution structures of relevant enzymes that bind PRibP provides evidence for the flexibility and importance of the compound in metabolism.

Summary: The importance of the microbiome to human health is increasingly recognized and has become a major focus of recent research. However, much of the work has focused on a few aspects, particularly the bacterial component of the microbiome, most frequently in the gastrointestinal tract. Yet humans and other animals can be colonized by a wide array of organisms spanning all domains of life, including bacteria and archaea, unicellular eukaryotes such as fungi, multicellular eukaryotes such as helminths, and viruses. As they share the same host niches, they can compete with, synergize with, and antagonize each other, with potential impacts on their host. Here, we discuss these major groups making up the human microbiome, with a focus on how they interact with each other and their multicellular host.