

Microbiology and Molecular Biology Reviews

A Publication of the American Society for Microbiology

VOLUME 70 • DECEMBER 2006 • NUMBER 4

CONTENTS/SUMMARIES

- Messing with Bacterial Quorum Sensing.** Juan E. González and Neela D. Keshavan 859–875

Summary: Quorum sensing is widely recognized as an efficient mechanism to regulate expression of specific genes responsible for communal behavior in bacteria. Several bacterial phenotypes essential for the successful establishment of symbiotic, pathogenic, or commensal relationships with eukaryotic hosts, including motility, exopolysaccharide production, biofilm formation, and toxin production, are often regulated by quorum sensing. Interestingly, eukaryotes produce quorum-sensing-interfering (QSI) compounds that have a positive or negative influence on the bacterial signaling network. This eukaryotic interference could result in further fine-tuning of bacterial quorum sensing. Furthermore, recent work involving the synthesis of structural homologs to the various quorum-sensing signal molecules has resulted in the development of additional QSI compounds that could be used to control pathogenic bacteria. The creation of transgenic plants that express bacterial quorum-sensing genes is yet another strategy to interfere with bacterial behavior. Further investigation on the manipulation of quorum-sensing systems could provide us with powerful tools against harmful bacteria.

- DNA Replication in the Archaea.** Elizabeth R. Barry and Stephen D. Bell 876–887

Summary: The archaeal DNA replication machinery bears striking similarity to that of eukaryotes and is clearly distinct from the bacterial apparatus. In recent years, considerable advances have been made in understanding the biochemistry of the archaeal replication proteins. Furthermore, a number of structures have now been obtained for individual components and higher-order assemblies of archaeal replication factors, yielding important insights into the mechanisms of DNA replication in both archaea and eukaryotes.

- The Bacterial Actin-Like Cytoskeleton.** Rut Carballido-López 888–909

Summary: Recent advances have shown conclusively that bacterial cells possess distant but true homologues of actin (MreB, ParM, and the recently uncovered MamK protein). Despite weak amino acid sequence similarity, MreB and ParM exhibit high structural homology to actin. Just like F-actin in eukaryotes, MreB and ParM assemble into highly dynamic filamentous structures in vivo and in vitro. MreB-like proteins are essential for cell viability and have been implicated in major cellular processes, including cell morphogenesis, chromosome segregation, and cell polarity. ParM (a plasmid-encoded actin homologue) is responsible for driving plasmid-DNA partitioning. The dynamic prokaryotic actin-like cytoskeleton is thought to serve as a central organizer for the targeting and accurate positioning of proteins and nucleoprotein complexes,

Continued on following page

thereby (and by analogy to the eukaryotic cytoskeleton) spatially and temporally controlling macromolecular trafficking in bacterial cells. In this paper, the general properties and known functions of the actin orthologues in bacteria are reviewed.

Stimulus Perception in Bacterial Signal-Transducing Histidine Kinases. Thorsten Mascher, John D. Helmann, and Gottfried Unden.

910–938

Summary: Two-component signal-transducing systems are ubiquitously distributed communication interfaces in bacteria. They consist of a histidine kinase that senses a specific environmental stimulus and a cognate response regulator that mediates the cellular response, mostly through differential expression of target genes. Histidine kinases are typically transmembrane proteins harboring at least two domains: an input (or sensor) domain and a cytoplasmic transmitter (or kinase) domain. They can be identified and classified by virtue of their conserved cytoplasmic kinase domains. In contrast, the sensor domains are highly variable, reflecting the plethora of different signals and modes of sensing. In order to gain insight into the mechanisms of stimulus perception by bacterial histidine kinases, we here survey sensor domain architecture and topology within the bacterial membrane, functional aspects related to this topology, and sequence and phylogenetic conservation. Based on these criteria, three groups of histidine kinases can be differentiated. (i) Periplasmic-sensing histidine kinases detect their stimuli (often small solutes) through an extracellular input domain. (ii) Histidine kinases with sensing mechanisms linked to the transmembrane regions detect stimuli (usually membrane-associated stimuli, such as ionic strength, osmolarity, turgor, or functional state of the cell envelope) via their membrane-spanning segments and sometimes via additional short extracellular loops. (iii) Cytoplasmic-sensing histidine kinases (either membrane anchored or soluble) detect cellular or diffusible signals reporting the metabolic or developmental state of the cell. This review provides an overview of mechanisms of stimulus perception for members of all three groups of bacterial signal-transducing histidine kinases.

How Phosphotransferase System-Related Protein Phosphorylation Regulates Carbohydrate Metabolism in Bacteria. Josef Deutscher, Christof Francke, and Pieter W. Postma

939–1031

Summary: The phosphoenolpyruvate (PEP):carbohydrate phosphotransferase system (PTS) is found only in bacteria, where it catalyzes the transport and phosphorylation of numerous monosaccharides, disaccharides, amino sugars, polyols, and other sugar derivatives. To carry out its catalytic function in sugar transport and phosphorylation, the PTS uses PEP as an energy source and phosphoryl donor. The phosphoryl group of PEP is usually transferred via four distinct proteins (domains) to the transported sugar bound to the respective membrane component(s) (EIIC and EIID) of the PTS. The organization of the PTS as a four-step phosphoryl transfer system, in which all P derivatives exhibit similar energy (phosphorylation occurs at histidyl or cysteyle residues), is surprising, as a single protein (or domain) coupling energy transfer and sugar phosphorylation would be sufficient for PTS function. A possible explanation for the complexity of the PTS was provided by the discovery that the PTS also carries out numerous regulatory functions. Depending on their phosphorylation state, the four proteins (domains) forming the PTS phosphorylation cascade (EI, HPr, EIIA, and EIIB) can phosphorylate or interact with numerous non-PTS proteins and thereby regulate their activity. In addition, in certain bacteria, one of the PTS components (HPr) is phosphorylated by ATP at a seryl residue, which increases the complexity of PTS-mediated regulation. In this review, we try to summarize the known protein phosphorylation-related regulatory functions of the PTS. As we shall see, the PTS regulation network not only controls carbohydrate uptake and metabolism but also interferes with the utilization of nitrogen and phosphorus and the virulence of certain pathogens.

Impact of Protein Kinase PKR in Cell Biology: from Antiviral to Antiproliferative Action. M. A. García, J. Gil, I. Ventoso, S. Guerra, E. Domingo, C. Rivas, and M. Esteban

1032–1060

Summary: The double-stranded RNA-dependent protein kinase PKR is a critical mediator of

the antiproliferative and antiviral effects exerted by interferons. Not only is PKR an effector molecule on the cellular response to double-stranded RNA, but it also integrates signals in response to Toll-like receptor activation, growth factors, and diverse cellular stresses. In this review, we provide a detailed picture on how signaling downstream of PKR unfolds and what are the ultimate consequences for the cell fate. PKR activation affects both transcription and translation. PKR phosphorylation of the alpha subunit of eukaryotic initiation factor 2 results in a blockade on translation initiation. However, PKR cannot avoid the translation of some cellular and viral mRNAs bearing special features in their 5' untranslated regions. In addition, PKR affects diverse transcriptional factors such as interferon regulatory factor 1, STATs, p53, activating transcription factor 3, and NF- κ B. In particular, how PKR triggers a cascade of events involving IKK phosphorylation of I κ B and NF- κ B nuclear translocation has been intensively studied. At the cellular and organism levels PKR exerts antiproliferative effects, and it is a key antiviral agent. A point of convergence in both effects is that PKR activation results in apoptosis induction. The extent and strength of the antiviral action of PKR are clearly understood by the findings that unrelated viral proteins of animal viruses have evolved to inhibit PKR action by using diverse strategies. The case for the pathological consequences of the antiproliferative action of PKR is less understood, but therapeutic strategies aimed at targeting PKR are beginning to offer promising results.

Uses for JNK: the Many and Varied Substrates of the c-Jun N-Terminal Kinases. Marie A. Bogoyevitch and Bostjan Kobe...

1061–1095

Summary: The c-Jun N-terminal kinases (JNKs) are members of a larger group of serine/threonine (Ser/Thr) protein kinases from the mitogen-activated protein kinase family. JNKs were originally identified as stress-activated protein kinases in the livers of cycloheximide-challenged rats. Their subsequent purification, cloning, and naming as JNKs have emphasized their ability to phosphorylate and activate the transcription factor c-Jun. Studies of c-Jun and related transcription factor substrates have provided clues about both the preferred substrate phosphorylation sequences and additional docking domains recognized by JNK. There are now more than 50 proteins shown to be substrates for JNK. These include a range of nuclear substrates, including transcription factors and nuclear hormone receptors, heterogeneous nuclear ribonucleoprotein K, and the Pol I-specific transcription factor TIF-IA, which regulates ribosome synthesis. Many nonnuclear substrates have also been characterized, and these are involved in protein degradation (e.g., the E3 ligase Itch), signal transduction (e.g., adaptor and scaffold proteins and protein kinases), apoptotic cell death (e.g., mitochondrial Bcl2 family members), and cell movement (e.g., paxillin, DCX, microtubule-associated proteins, the stathmin family member SCG10, and the intermediate filament protein keratin 8). The range of JNK actions in the cell is therefore likely to be complex. Further characterization of the substrates of JNK should provide clearer explanations of the intracellular actions of the JNKs and may allow new avenues for targeting the JNK pathways with therapeutic agents downstream of JNK itself.