How Bacteria Consume Their Own Exoskeletons (Turnover and Recycling of Cell Wall Peptidoglycan).

James T. Park and Tsuyoshi Uehara

Summary: The phenomenon of peptidoglycan recycling is reviewed. Gram-negative bacteria such as Escherichia coli break down and reuse over 60% of the peptidoglycan of their side wall each generation. Recycling of newly made peptidoglycan during septum synthesis occurs at an even faster rate. Nine enzymes, one permease, and one periplasmic binding protein in E. coli that appear to have as their sole function the recovery of degradation products from peptidoglycan, thereby making them available for the cell to resynthesize more peptidoglycan or to use as an energy source, have been identified. It is shown that all of the amino acids and amino sugars of peptidoglycan are recycled. The discovery and properties of the individual proteins and the pathways involved are presented. In addition, the possible role of various peptidoglycan degradation products in the induction of β-lactamase is discussed.

Evolutionary Persistence of the Molybdopyranopterin-Containing Sulfite Oxidase Protein Fold.

Gregory J. Workun, Kamila Moquin, Richard A. Rothery, and Joel H. Weiner

Summary: The importance of molybdoenzymes is exemplified both by the debilitating and fatal human diseases caused by their deficiency and by their persistence throughout evolution. Here, we show that the protein fold of the molybdopyranopterin-containing domain of sulfite oxidase (the SUOX fold) can be found in all three domains of life. Analyses of sequence data and protein structure comparisons (secondary structure matching) show that the SUOX fold is found in enzymes that have quite distinct macromolecular architectures comprising one or more domains and sometimes subsidiary subunits. These are summarized as follows: (i) animal SUOXs that contain an N-terminal cytochrome b5 domain and an SUOX fold fused to a C-terminal dimerization domain; (ii) plant SUOX that contains an SUOX fold fused to a C-terminal dimerization domain; (iii) the YedY protein from Escherichia coli, which comprises only the SUOX fold; (iv) the sulfite dehydrogenase from Starkeya novella that contains the SUOX fold, a dimerization domain, and an additional c-type cytochrome subunit; and (v) the plant-type nitrate reductases, exemplified by that of Pichia angusta, that contain an N-terminal SUOX fold, a dimerization domain, a cytochrome b5 domain, and a C-terminal NADH binding flavin adenine dinucleotide-containing domain. We used the primary sequences of the proteins containing an SUOX fold to mine 559 sequences of related proteins. A phylogeny of a nonredundant subset of these sequences was generated, and the resultant clades were categorized by sequence motif analyses in the context of the available protein structures. Based on the motif analyses, cladistics, and domain conservations, we are able to postulate a plausible pathway of SUOX fold enzyme evolution.
Tegument Proteins of Human Cytomegalovirus. Robert F. Kalejta 249–265

Summary: Human cytomegalovirus (HCMV) is a common, medically relevant human herpesvirus. The tegument layer of herpesvirus virions lies between the genome-containing capsids and the viral envelope. Proteins within the tegument layer of herpesviruses are released into the cell upon entry when the viral envelope fuses with the cell membrane. These proteins are fully formed and active and control viral entry, gene expression, and immune evasion. Most tegument proteins accumulate to high levels during later stages of infection, when they direct the assembly and egress of progeny virions. Thus, viral tegument proteins play critical roles at the very earliest and very last steps of the HCMV lytic replication cycle. This review summarizes HCMV tegument composition and structure as well as the known and speculated functions of viral tegument proteins. Important directions for future investigation and the challenges that lie ahead are identified and discussed.

Regulation of Pyrimidine Biosynthetic Gene Expression in Bacteria: Repression without Repressors. Charles L. Turnbough, Jr., and Robert L. Switzer 266–300

Summary: DNA-binding repressor proteins that govern transcription initiation in response to end products generally regulate bacterial biosynthetic genes, but this is rarely true for the pyrimidine biosynthetic (pyr) genes. Instead, bacterial pyr gene regulation generally involves mechanisms that rely only on regulatory sequences embedded in the leader region of the operon, which cause premature transcription termination or translation inhibition in response to nucleotide signals. Studies with Escherichia coli and Bacillus subtilis pyr genes reveal a variety of regulatory mechanisms. Transcription attenuation via UTP-sensitive coupled transcription and translation regulates expression of the pyrBI and pyrE operons in enteric bacteria, whereas nucleotide effects on binding of the PyrR protein to pyr mRNA attenuation sites control pyr operon expression in most gram-positive bacteria. Nucleotide-sensitive reiterative transcription underlies regulation of other pyr genes. With the E. coli pyrBI, carAB, codBA, and upp-uraA operons, UTP-sensitive reiterative transcription within the initially transcribed region (ITR) leads to nonproductive transcription initiation. CTP-sensitive reiterative transcription in the pyrG ITRs of gram-positive bacteria, which involves the addition of G residues, results in the formation of an antiterminator RNA hairpin and suppression of transcription attenuation. Some mechanisms involve regulation of translation rather than transcription. Expression of the pyrC and pyrD operons of enteric bacteria is controlled by nucleotide-sensitive transcription start switching that produces transcripts with different potentials for translation. In Mycobacterium smegmatis and other bacteria, PyrR modulates translation of pyr genes by binding to their ribosome binding site. Evidence supporting these conclusions, generalizations for other bacteria, and prospects for future research are presented.

Structural Biology of Pectin Degradation by Enterobacteriaceae. D. Wade Abbott and Alisdair B. Boraston 301–316

Summary: Pectin is a structural polysaccharide that is integral for the stability of plant cell walls. During soft rot infection, secreted virulence factors from pectinolytic bacteria such as Erwinia spp. degrade pectin, resulting in characteristic plant cell necrosis and tissue maceration. Catabolism of pectin and its breakdown products by pectinolytic bacteria occurs within distinct cellular environments. This process initiates outside the cell, continues within the periplasmic space, and culminates in the cytoplasm. Although pectin utilization is well understood at the genetic and biochemical levels, an inclusive structural description of pectinases and pectin binding proteins by both extracellular and periplasmic enzymes has been lacking, especially following the recent characterization of several periplasmic components and protein-oligogalacturonide complexes. Here we provide a comprehensive analysis of the protein folds and mechanisms of pectate lyases, polygalacturonases, and carbohydrate esterases and the binding specificities of two periplasmic pectin binding proteins from Enterobacteriaceae. This review provides a structural understanding of the molecular determinants of pectin utilization and the mechanisms driving catabolite selectivity and flow through the pathway.

Summary: ATP-binding cassette (ABC) systems are universally distributed among living organisms and function in many different aspects of bacterial physiology. ABC transporters are best known for their role in the import of essential nutrients and the export of toxic molecules, but they can also mediate the transport of many other physiological substrates. In a classical transport reaction, two highly conserved ATP-binding domains or subunits couple the binding/hydrolysis of ATP to the translocation of particular substrates across the membrane, through interactions with membrane-spanning domains of the transporter. Variations on this basic theme involve soluble ABC ATP-binding proteins that couple ATP hydrolysis to nontransport processes, such as DNA repair and gene expression regulation. Insights into the structure, function, and mechanism of action of bacterial ABC proteins are reported, based on phylogenetic comparisons as well as classic biochemical and genetic approaches. The availability of an increasing number of high-resolution structures has provided a valuable framework for interpretation of recent studies, and realistic models have been proposed to explain how these fascinating molecular machines use complex dynamic processes to fulfill their numerous biological functions. These advances are also important for elucidating the mechanism of action of eukaryotic ABC proteins, because functional defects in many of them are responsible for severe human inherited diseases.


Summary: Plasmid R124 was first described in 1972 as being a new member of incompatibility group IncFIV, yet early physical investigations of plasmid DNA showed that this type of classification was more complex than first imagined. Throughout the history of the study of this plasmid, there have been many unexpected observations. Therefore, in this review, we describe the history of our understanding of this plasmid and the type I restriction-modification (R-M) system that it encodes, which will allow an opportunity to correct errors, or misunderstandings, that have arisen in the literature. We also describe the characterization of the R-M enzyme EcoR124I and describe the unusual properties of both type I R-M enzymes and EcoR124I in particular. As we approached the 21st century, we began to see the potential of the EcoR124I R-M enzyme as a useful molecular motor, and this leads to a description of recent work that has shown that the R-M enzyme can be used as a nanoactuator. Therefore, this is a history that takes us from a plasmid isolated from (presumably) an infected source to the potential use of the plasmid-encoded R-M enzyme in bionanotechnology.

ERRATUM

The Membrane-Proximal External Region of the Human Immunodeficiency Virus Type 1 Envelope: Dominant Site of Antibody Neutralization and Target for Vaccine Design. Marinieve Montero, Nienke E. van Houten, Xin Wang, and Jamie K. Scott ................................. 378

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