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CONTENTS/SUMMARIES

Carbohydrate Binding Modules: Biochemical Properties and Novel Applications. Oded Shoseyov, Ziv Shani, and Ilan Levy 283–295

Summary: Polysaccharide-degrading microorganisms express a repertoire of hydrolytic enzymes that act in synergy on plant cell wall and other natural polysaccharides to elicit the degradation of often-recalcitrant substrates. These enzymes, particularly those that hydrolyze cellulose and hemicellulose, have a complex molecular architecture comprising discrete modules which are normally joined by relatively unstructured linker sequences. This structure is typically comprised of a catalytic module and one or more carbohydrate binding modules (CBMs) that bind to the polysaccharide. CBMs, by bringing the biocatalyst into intimate and prolonged association with its substrate, allow and promote catalysis. Based on their properties, CBMs are grouped into 43 families that display substantial variation in substrate specificity, along with other properties that make them a gold mine for biotechnologists who seek natural molecular “Velcro” for diverse and unusual applications. In this article, we review recent progress in the field of CBMs and provide an up-to-date summary of the latest developments in CBM applications.

ISCR Elements: Novel Gene-Capturing Systems of the 21st Century? Mark A. Toleman, Peter M. Bennett, and Timothy R. Walsh 296–316

Summary: “Common regions” (CRs), such as Orf513, are being increasingly linked to mega-antibiotic-resistant regions. While their overall nucleotide sequences show little identity to other mobile elements, amino acid alignments indicate that they possess the key motifs of IS91-like elements, which have been linked to the mobility ent plasmids in pathogenic Escherichia coli. Further inspection reveals that they possess an IS91-like origin of replication and termination sites (terIS), and therefore CRs probably transpose via a rolling-circle replication mechanism. Accordingly, in this review we have renamed CRs as ISCRs to give a more accurate reflection of their functional properties. The genetic context surrounding ISCRs indicates that they can procure 5' sequences via misreading of the cognate terIS, i.e., “unchecked transposition.” Clinically, the most worrying aspect of ISCRs is that they are increasingly being linked with more potent examples of resistance, i.e., metallo- β -lactamases in Pseudomonas aeruginosa and co-trimoxazole resistance in Stenotrophomonas maltophilia. Furthermore, if ISCR elements do move via “unchecked RC transposition,” as has been speculated for ISCR1, then this mechanism provides antibiotic resistance genes with a highly mobile genetic vehicle that could greatly exceed the effects of previously reported mobile genetic mechanisms. It has been hypothesized that bacteria will surprise us by extending their “genetic construction kit” to procure and evince additional DNA and, therefore, antibiotic resistance genes. It appears that ISCR elements have now firmly established themselves within that regimen.

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Cell Wall Assembly in *Saccharomyces cerevisiae*. Guillaume Lesage and Howard Bussey 317–343

*Summary: An extracellular matrix composed of a layered meshwork of β -glucans, chitin, and mannoproteins encapsulates cells of the yeast *Saccharomyces cerevisiae*. This organelle determines cellular morphology and plays a critical role in maintaining cell integrity during cell growth and division, under stress conditions, upon cell fusion in mating, and in the durable ascospore cell wall. Here we assess recent progress in understanding the molecular biology and biochemistry of cell wall synthesis and its remodeling in *S. cerevisiae*. We then review the regulatory dynamics of cell wall assembly, an area where functional genomics offers new insights into the integration of cell wall growth and morphogenesis with a polarized secretory system that is under cell cycle and cell type program controls.*

Defenses against Oxidative Stress in *Neisseria gonorrhoeae*: a System Tailored for a Challenging Environment. Kate L. Seib, Hsing-Ju Wu, Stephen P. Kidd, Michael A. Apicella, Michael P. Jennings, and Alastair G. McEwan..... 344–361

*Summary: *Neisseria gonorrhoeae* is a host-adapted pathogen that colonizes primarily the human genitourinary tract. This bacterium encounters reactive oxygen and reactive nitrogen species as a consequence of localized inflammatory responses in the urethra of males and endocervix of females and also of the activity of commensal lactobacilli in the vaginal flora. This review describes recent advances in the understanding of defense systems against oxidative stress in *N. gonorrhoeae* and shows that while some of its defenses have similarities to the paradigm established with *Escherichia coli*, there are also some key differences. These differences include the presence of a defense system against superoxide based on manganese ions and a glutathione-dependent system for defense against nitric oxide which is under the control of a novel MerR-like transcriptional regulator. An understanding of the defenses against oxidative stress in *N. gonorrhoeae* and their regulation may provide new insights into the ways in which this bacterium survives challenges from polymorphonuclear leukocytes and urogenital epithelial cells.*

The *Escherichia coli* Proteome: Past, Present, and Future Prospects. Mee-Jung Han and Sang Yup Lee..... 362–439

*Summary: Proteomics has emerged as an indispensable methodology for large-scale protein analysis in functional genomics. The *Escherichia coli* proteome has been extensively studied and is well defined in terms of biochemical, biological, and biotechnological data. Even before the entire *E. coli* proteome was fully elucidated, the largest available data set had been integrated to decipher regulatory circuits and metabolic pathways, providing valuable insights into global cellular physiology and the development of metabolic and cellular engineering strategies. With the recent advent of advanced proteomic technologies, the *E. coli* proteome has been used for the validation of new technologies and methodologies such as sample prefractionation, protein enrichment, two-dimensional gel electrophoresis, protein detection, mass spectrometry (MS), combinatorial assays with n-dimensional chromatographies and MS, and image analysis software. These important technologies will not only provide a great amount of additional information on the *E. coli* proteome but also synergistically contribute to other proteomic studies. Here, we review the past development and current status of *E. coli* proteome research in terms of its biological, biotechnological, and methodological significance and suggest future prospects.*

Regulation of the Cell Cycle by Protein Phosphatase 2A in *Saccharomyces cerevisiae*. Yu Jiang 440–449

*Summary: Protein phosphatase 2A (PP2A) has long been implicated in cell cycle regulation in many different organisms. In the yeast *Saccharomyces cerevisiae*, PP2A controls cell cycle progression mainly through modulation of cyclin-dependent kinase (CDK) at the G_2/M tran-*

sition. However, CDK does not appear to be a direct target of PP2A. PP2A affects CDK activity through its roles in checkpoint controls. Inactivation of PP2A downregulates CDK by activating the morphogenesis checkpoint and, consequently, delays mitotic entry. Defects in PP2A also compromise the spindle checkpoint and predispose the cell to an error-prone mitotic exit. In addition, PP2A is involved in controlling the G₁/S transition and cytokinesis. These findings suggest that PP2A functions in many stages of the cell cycle and its effect on cell cycle progression is pleiotropic.

Plant Pathogen Forensics: Capabilities, Needs, and Recommendations. J. Fletcher, C. Bender, B. Budowle, W. T. Cobb, S. E. Gold, C. A. Ishimaru, D. Luster, U. Melcher, R. Murch, H. Scherm, R. C. Seem, J. L. Sherwood, B. W. Sobral, and S. A. Tolin 450–471

Summary: A biological attack on U.S. crops, rangelands, or forests could reduce yield and quality, erode consumer confidence, affect economic health and the environment, and possibly impact human nutrition and international relations. Preparedness for a crop bioterror event requires a strong national security plan that includes steps for microbial forensics and criminal attribution. However, U.S. crop producers, consultants, and agricultural scientists have traditionally focused primarily on strategies for prevention and management of diseases introduced naturally or unintentionally rather than on responding appropriately to an intentional pathogen introduction. We assess currently available information, technologies, and resources that were developed originally to ensure plant health but also could be utilized for postintroduction plant pathogen forensics. Recommendations for prioritization of efforts and resource expenditures needed to enhance our plant pathogen forensics capabilities are presented.

Cyanobacterial Two-Component Proteins: Structure, Diversity, Distribution, and Evolution. Mark K. Ashby and Jean Houmard 472–509

Summary: A survey of the already characterized and potential two-component protein sequences that exist in the nine complete and seven partially annotated cyanobacterial genome sequences available (as of May 2005) showed that the cyanobacteria possess a much larger repertoire of such proteins than most other bacteria. By analysis of the domain structure of the 1,171 potential histidine kinases, response regulators, and hybrid kinases, many various arrangements of about thirty different modules could be distinguished. The number of two-component proteins is related in part to genome size but also to the variety of physiological properties and ecophysiologicals of the different strains. Groups of orthologues were defined, only a few of which have representatives with known physiological functions. Based on comparisons with the proposed phylogenetic relationships between the strains, the orthology groups show that (i) a few genes, some of them clustered on the genome, have been conserved by all species, suggesting their very ancient origin and an essential role for the corresponding proteins, and (ii) duplications, fusions, gene losses, insertions, and deletions, as well as domain shuffling, occurred during evolution, leading to the extant repertoire. These mechanisms are put in perspective with the different genetic properties that cyanobacteria have to achieve genome plasticity. This review is designed to serve as a basis for orienting further research aimed at defining the most ancient regulatory mechanisms and understanding how evolution worked to select and keep the most appropriate systems for cyanobacteria to develop in the quite different environments that they have successfully colonized.

Biology of *Pseudomonas stutzeri*. Jorge Lalucat, Antoni Bennisar, Rafael Bosch, Elena García-Valdés, and Norberto J. Palleroni 510–547

Summary: Pseudomonas stutzeri is a nonfluorescent denitrifying bacterium widely distributed in the environment, and it has also been isolated as an opportunistic pathogen from humans. Over the past 15 years, much progress has been made in elucidating the taxonomy of this diverse taxonomical group, demonstrating the clonality of its populations. The species has received much attention because of its particular metabolic properties: it has been proposed as a model organism for denitrification studies; many strains have natural transformation properties, making it relevant for study of the transfer of genes in the environment; several strains are able

to fix dinitrogen; and others participate in the degradation of pollutants or interact with toxic metals. This review considers the history of the discovery, nomenclatural changes, and early studies, together with the relevant biological and ecological properties, of *P. stutzeri*.

Human Immunodeficiency Virus Type 1 Nef: Adapting to Intracellular Trafficking Pathways. Jeremiah F. Roeth and Kathleen L. Collins.....

548-563

Summary: The Nef protein of primate lentiviruses is a unique protein that has evolved in several ways to manipulate the biology of an infected cell to support viral replication, immune evasion, pathogenesis, and viral spread. Nef is a small (25- to 34-kDa), myristoylated protein that binds to a collection of cellular factors and acts as an adaptor to generate novel protein interactions to accomplish specific functions. Of the many biological activities attributed to Nef, the reduction of surface levels of the viral receptor (CD4) and antigen-presenting molecules (major histocompatibility complex class I) has been intensely examined; recent evidence demonstrates that Nef utilizes multiple, distinct pathways to affect these proteins. To accomplish this, Nef promotes the formation of multiprotein complexes, recruiting host adaptor proteins to commandeered intracellular vesicular trafficking routes. The altered trafficking of several other host molecules has also been reported, and an emerging theory suggests that Nef generates pleiotropic effects in the secretory and endocytic pathways that reprogram intracellular protein trafficking and may ultimately provide an efficient platform for viral assembly. This review critically discusses some of the major findings regarding the impact of human immunodeficiency virus type 1 Nef on host protein transport and addresses some emerging directions in this area of human immunodeficiency virus biology.

The Continuing Story of Class IIa Bacteriocins. Djamel Drider, Gunnar Fimland, Yann Héchar, Lynn M. McMullen, and Hervé Prévost.....

564-582

*Summary: Many bacteria produce antimicrobial peptides, which are also referred to as peptide bacteriocins. The class IIa bacteriocins, often designated pediocin-like bacteriocins, constitute the most dominant group of antimicrobial peptides produced by lactic acid bacteria. The bacteriocins that belong to this class are structurally related and kill target cells by membrane permeabilization. Despite their structural similarity, class IIa bacteriocins display different target cell specificities. In the search for new antibiotic substances, the class IIa bacteriocins have been identified as promising new candidates and have thus received much attention. They kill some pathogenic bacteria (e.g., *Listeria*) with high efficiency, and they constitute a good model system for structure-function analyses of antimicrobial peptides in general. This review focuses on class IIa bacteriocins, especially on their structure, function, mode of action, biosynthesis, bacteriocin immunity, and current food applications. The genetics and biosynthesis of class IIa bacteriocins are well understood. The bacteriocins are ribosomally synthesized with an N-terminal leader sequence, which is cleaved off upon secretion. After externalization, the class IIa bacteriocins attach to potential target cells and, through electrostatic and hydrophobic interactions, subsequently permeabilize the cell membrane of sensitive cells. Recent observations suggest that a chiral interaction and possibly the presence of a mannose permease protein on the target cell surface are required for a bacteria to be sensitive to class IIa bacteriocins. There is also substantial evidence that the C-terminal half penetrates into the target cell membrane, and it plays an important role in determining the target cell specificity of these bacteriocins. Immunity proteins protect the bacteriocin producer from the bacteriocin it secretes. The three-dimensional structures of two class IIa immunity proteins have been determined, and it has been shown that the C-terminal halves of these cytosolic four-helix bundle proteins specify which class IIa bacteriocin they protect against.*