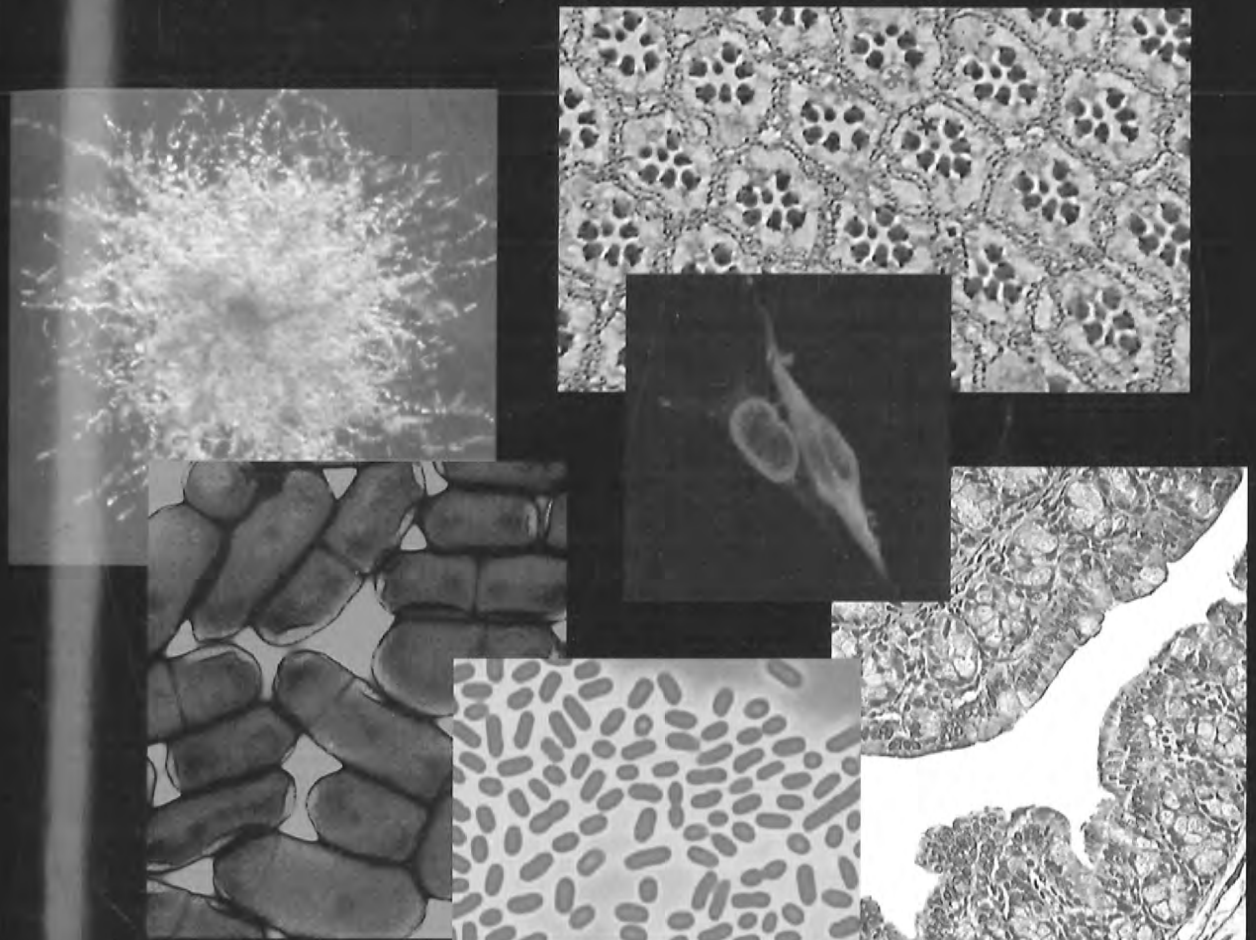
mmbr

MICROBIOLOGY AND MOLECULAR BIOLOGY REVIEWS

SEPTEMBER 2003 • VOL. 67, NO. 3



MICROBIOLOGY AND MOLECULAR BIOLOGY REVIEWS

VOLUME 67 • SEPTEMBER 2003 • NUMBER 3

Microbiology and Molecular Biology Reviews considers for publication both solicited and unsolicited reviews and monographs dealing with all aspects of microbiology. Manuscripts, proposals, and correspondence regarding editorial matters should be addressed to the Editor in Chief, Jack D. Keene, Department of Microbiology, Box 3020, Duke University Medical Center, Durham, NC 27710; phone (919) 684-5138; fax (919) 684-8735.

Microbiology and Molecular Biology Reviews (ISSN 1092-2172) is published quarterly (March, June, September, and December), one volume per year, by the American Society for Microbiology (ASM), 1752 N St., N.W., Washington, DC 20036-2904. Nonmember print subscription prices (per year) are: $358, U.S.; $363, Canada (plus 7% GST, or 7% GST + 8% HST where applicable); $371, Europe; $374, Latin America; $375, rest of world. Member print subscription prices (per year) are: $52, U.S.; $63, Canada (plus 7% GST, or 7% GST + 8% HST where applicable); $65, Europe; $70, Latin America; $70, rest of world. Single copies are: $50, nonmember; $25, member (Canadians add 7% GST, or 7% GST + 8% HST where applicable). For prices of electronic versions, contact the Subscriptions Unit, ASM. Correspondence relating to subscriptions, defective copies, missing issues, and availability of back issues should be directed to the Subscriptions Unit, ASM; correspondence relating to reprint orders should be directed to the Reprint Order Unit, ASM; and correspondence relating to disposition of proofs and general editorial matters should be directed to the Journals Department, American Society for Microbiology, 1752 N St., N.W., Washington, DC 20036-2904. Phone: (202) 737-3600.

Claims for missing issues from residents of the United States, Canada, and Mexico must be submitted within 3 months after publication of the issues; residents of all other countries must submit claims within 6 months of publication of the issues. Claims for issues missing because of failure to report an address change or for issues "missing from files" will not be allowed.

Periodicals postage paid at Washington, DC 20036, and at additional mailing offices.

POSTMASTER: Send address changes to *Microbiology and Molecular Biology Reviews*, ASM, 1752 N St., N.W., Washington, DC 20036-2904.

Made in the United States of America. Printed on acid-free paper. DOI: 10.1128/MMBR.67.3.2003 CODEN: MMBRF7

CONTENTS/SUMMARIES

Ancient Origin of the Tryptophan Operon and the Dynamics of Evolutionary Change. Gary Xie, Nemat O. Keyhani, Carol A. Bonner, and Roy A. Jensen 303–342

Summary: The seven conserved enzymatic domains required for tryptophan (Trp) biosynthesis are encoded in seven genetic regions that are organized differently (whole-pathway operons, multiple partial-pathway operons, and dispersed genes) in prokaryotes. A comparative bioinformatics evaluation of the conservation and organization of the genes of Trp biosynthesis in prokaryotic operons should serve as an excellent model for assessing the feasibility of predicting the evolutionary histories of genes and operons associated with other biochemical pathways. These comparisons should provide a better understanding of possible explanations for differences in operon organization in different organisms at a genomics level. These analyses may also permit identification of some of the prevailing forces that dictated specific gene rearrangements during the course of evolution. Operons concerned with Trp biosynthesis in prokaryotes have been in a dynamic state of flux. Analysis of closely related organisms among the Bacteria at various phylogenetic nodes reveals many examples of operon scission, gene dispersal, gene fusion, gene scrambling, and gene loss from which the direction of evolutionary events can be deduced. Two milestone evolutionary events have been mapped to the 16S rRNA tree of Bacteria, one splitting the operon in two, and the other rejoining it by gene fusion. The Archaea, though less resolved due to a lesser genome representation, appear to exhibit more gene scrambling than the Bacteria. The trp operon appears to have been an ancient innovation; it was already present in the common ancestor of Bacteria and Archaea. Although the operon has been subjected, even in recent times, to dynamic changes in gene rearrangement, the ancestral gene order can be deduced with confidence. The evolutionary history of the genes of the pathway is discernible in rough outline as a vertical line of descent, with events of lateral gene transfer or paralogy enriching the analysis as interesting features that can be distinguished. As additional genomes are thoroughly analyzed, an increasingly refined resolution of the sequential evolutionary steps is clearly possible. These comparisons suggest that present-day trp operons that possess finely tuned regulatory features are under strong positive selection and are able to resist the disruptive evolutionary events that may be experienced by simpler, poorly regulated operons.

RNA Binding Protein Sex-Lethal (Sxl) and Control of *Drosophila* Sex Determination and Dosage Compensation. Luiz O. F. Penalva and Lucas Sánchez 343–359

Summary: In the past two decades, scientists have elucidated the molecular mechanisms behind Drosophila sex determination and dosage compensation. These two processes are controlled essentially by two different sets of genes, which have in common a master regulatory gene, Sex-lethal (Sxl). Sxl encodes one of the best-characterized members of the family of RNA

Continued on following page

Continued from preceding page

binding proteins. The analysis of different mechanisms involved in the regulation of the three identified Sxl target genes (Sex-lethal itself, transformer, and male specific lethal-2) has contributed to a better understanding of translation repression, as well as constitutive and alternative splicing. Studies using the Drosophila system have identified the features of the protein that contribute to its target specificity and regulatory functions. In this article, we review the existing data concerning Sxl protein, its biological functions, and the regulation of its target genes.

Repetitive Elements in Genomes of Parasitic Protozoa. Bill Wickstead, Klaus Ersfeld, and Keith Gull 360–375

Summary: Repetitive DNA elements have been a part of the genomic fauna of eukaryotes perhaps since their very beginnings. Millions of years of coevolution have given repeats central roles in chromosome maintenance and genetic modulation. Here we review the genomes of parasitic protozoa in the context of the current understanding of repetitive elements. Particular reference is made to repeats in five medically important species with ongoing or completed genome sequencing projects: Plasmodium falciparum, Leishmania major, Trypanosoma brucei, Trypanosoma cruzi, and Giardia lamblia. These organisms are used to illustrate five thematic classes of repeats with different structures and genomic locations. We discuss how these repeat classes may interact with parasitic life-style and also how they can be used as experimental tools. The story which emerges is one of opportunism and upheaval which have been employed to add genetic diversity and genomic flexibility.

Longevity Regulation in *Saccharomyces cerevisiae*: Linking Metabolism, Genome Stability, and Heterochromatin. Kevin J. Bitterman, Oliver Medvedik, and David A. Sinclair 376–399

Summary: When it was first proposed that the budding yeast Saccharomyces cerevisiae might serve as a model for human aging in 1959, the suggestion was met with considerable skepticism. Although yeast had proved a valuable model for understanding basic cellular processes in humans, it was difficult to accept that such a simple unicellular organism could provide information about human aging, one of the most complex of biological phenomena. While it is true that causes of aging are likely to be multifarious, there is a growing realization that all eukaryotes possess surprisingly conserved longevity pathways that govern the pace of aging. This realization has come, in part, from studies of S. cerevisiae, which has emerged as a highly informative and respected model for the study of life span regulation. Genomic instability has been identified as a major cause of aging, and over a dozen longevity genes have now been identified that suppress it. Here we present the key discoveries in the yeast-aging field, regarding both the replicative and chronological measures of life span in this organism. We discuss the implications of these findings not only for mammalian longevity but also for other key aspects of cell biology, including cell survival, the relationship between chromatin structure and genome stability, and the effect of internal and external environments on cellular defense pathways. We focus on the regulation of replicative life span, since recent findings have shed considerable light on the mechanisms controlling this process. We also present the specific methods used to study aging and longevity regulation in S. cerevisiae.

***Candida albicans* Secreted Aspartyl Proteinases in Virulence and Pathogenesis.** Julian R. Naglik, Stephen J. Challacombe, and Bernhard Hube 400–428

contribute to Candida virulence and pathogenesis.

Surviving the Acid Test: Responses of Gram-Positive Bacteria to Low pH. Paul D. Cotter and Colin Hill 429–453

Summary: Gram-positive bacteria possess a myriad of acid resistance systems that can help them to overcome the challenge posed by different acidic environments. In this review the most common mechanisms are described: i.e., the use of proton pumps, the protection or repair of macromolecules, cell membrane changes, production of alkali, induction of pathways by transcriptional regulators, alteration of metabolism, and the role of cell density and cell signaling. We also discuss the reponses of Listeria monocytogenes, Rhodococcus, Mycobacterium, Clostridium perfringens, Staphylococcus aureus, Bacillus cereus, oral streptococci, and lactic acid bacteria to acidic environments and outline ways in which this knowledge has been or may be used to either aid or prevent bacterial survival in low-pH environments.

Transmembrane Movement of Long-Chain Fatty Acids. Paul N. Black and Concetta C. DiRusso 454–472

Summary: The processes that govern the regulated transport of long-chain fatty acids across the plasma membrane are quite distinct compared to counterparts involved in the transport of hydrophilic solutes such as sugars and amino acids. These differences stem from the unique physical and chemical properties of long-chain fatty acids. To date, several distinct classes of proteins have been shown to participate in the transport of exogenous long-chain fatty acids across the membrane. More recent work is consistent with the hypothesis that in addition to the role played by proteins in this process, there is a diffusional component which must also be considered. Central to the development of this hypothesis are the appropriate experimental systems, which can be manipulated using the tools of molecular genetics. Escherichia coli and Saccharomyces cerevisiae are ideally suited as model systems to study this process in that both (i) exhibit saturable long-chain fatty acid transport at low ligand concentrations, (ii) have specific membrane-bound and membrane-associated proteins that are components of the transport apparatus, and (iii) can be easily manipulated using the tools of molecular genetics. In both systems, central players in the process of fatty acid transport are fatty acid transport proteins (FadL or Fat1p) and fatty acyl coenzyme A (CoA) synthetase (FACS; fatty acid CoA ligase [AMP forming] [EC 6.2.1.3]). FACS appears to function in concert with FadL (bacteria) or Fat1p (yeast) in the conversion of the free fatty acid to CoA thioesters concomitant with transport, thereby rendering this process unidirectional. This process of trapping transported fatty acids represents one fundamental mechanism operational in the transport of exogenous fatty acids.

ERRATUM

Prophage Genomics. Carlos Canchaya, Caroline Proux, Ghislain Fournous, Anne Bruttin, and Harald Brüssow 473

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.