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<table>
<thead>
<tr>
<th>Title</th>
<th>Authors</th>
<th>Page No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>On the early dynamics and spread of HIV-1</td>
<td>Brittany Rife, Marco Salemi</td>
<td>01</td>
</tr>
<tr>
<td>Cell-size maintenance: universal strategy revealed</td>
<td>Suckjoon Jun, Sattar Taheri-Araghi</td>
<td>01</td>
</tr>
<tr>
<td>Bridging the gap between viable but non-culturable and antibiotic persistent bacteria</td>
<td>Mesrop Ayrapetyan, Tiffany C. Williams, James D. Oliver</td>
<td>01</td>
</tr>
<tr>
<td>Diversity and disease pathogenesis in Mycobacterium tuberculosis</td>
<td>Digby F. Warner, Anastasia Koch, Valerie Mizrahi</td>
<td>01</td>
</tr>
<tr>
<td>Bacterial microcompartments and the modular construction of microbial metabolism</td>
<td>Cheryl A. Kerfeld, Onur Erbilgin</td>
<td>02</td>
</tr>
<tr>
<td>Arthritogenic alphaviruses: new insights into arthritis and bone pathology</td>
<td>Weiqiang Chen, Suan-Sin Foo, Natalie A. Sims, Lara J. Herrero, Nicole C. Walsh, Suresh Mahalingam</td>
<td>02</td>
</tr>
<tr>
<td>Multidrug resistance genes in staphylococci from animals that confer resistance to critically and highly important antimicrobial agents in human medicine</td>
<td>Sarah Wendlandt, Jianzhong Shen, Kristina Kadlec, Yang Wang, Beibei Li, Wan-Jiang Zhang, Andrea T. Feßler, Congming Wu, Stefan Schwarz</td>
<td>02</td>
</tr>
<tr>
<td>Response of host inflammasomes to viral infection</td>
<td>I-Yin Chen, Takeshi Ichinohe</td>
<td>03</td>
</tr>
<tr>
<td>A race for an Ebola vaccine: promises and obstacles</td>
<td></td>
<td>03</td>
</tr>
<tr>
<td>Success in incorporating horizontally transferred genes: the H-NS protein</td>
<td>Mario Hüttener, Sonia Paytubi, Antonio Juárez</td>
<td>03</td>
</tr>
<tr>
<td>Transmission of antimicrobial resistance in resource-poor healthcare</td>
<td>Jodi A. Lindsay</td>
<td>03</td>
</tr>
<tr>
<td>Solving the etiology of dental caries</td>
<td>Aurea Simón-Soro, Alex Mira</td>
<td>03</td>
</tr>
<tr>
<td>Elite control of HIV: is this the right model for a functional cure?</td>
<td>Leslie R. Cockerham, Hiroyu Hatano</td>
<td>04</td>
</tr>
<tr>
<td>Viral biocontrol: grand experiments in disease emergence and evolution</td>
<td>Francesca Di Giallonardo, Edward C. Holmes</td>
<td>04</td>
</tr>
<tr>
<td>Light-driven ion-translocating rhodopsins in marine bacteria</td>
<td>Keiichi Inoue, Yoshitaka Kato, Hideki Kandori</td>
<td>04</td>
</tr>
</tbody>
</table>
Understanding carbon catabolite repression in Escherichia coli using quantitative models
A. Kremling, J. Geiselmann, D. Ropers, H. de Jong

Nucleoside antibiotics: biosynthesis, regulation, and biotechnology
Guoqing Niu, Huarong Tan

Volume 23, Issue 3, March 2015

Following the equator: division site selection in Streptococcus pneumoniae
Marc Bramkamp

Architectural plan of transcriptional regulation in Mycobacterium tuberculosis
Priyanka Baloni, Nagasuma Chandra

Is selection relevant in the evolutionary emergence of drug resistance?
Troy Day, Silvie Huijben, Andrew F. Read

The demographic determinants of human microbiome health
Sylvie Estrela, Marvin Whiteley, Sam P. Brown

Reverse zoonosis of influenza to swine: new perspectives on the human–animal interface
Martha I. Nelson, Amy L. Vincent

Mx GTPases: dynamin-like antiviral machines of innate immunity
Otto Haller, Peter Staeheli, Martin Schwemmle, Georg Kochs

The general stress response in Alphaproteobacteria
Anne Francez-Charlot, Andreas Kazmarchczyk, Hans-Martin Fischer, Julia A. Vorholt

Bats as ‘special’ reservoirs for emerging zoonotic pathogens
Cara E. Brook, Andrew P. Dobson

Volume 23, Issue 4, April 2015

Meningitis in adolescents: the role of commensal microbiota
James W.B. Moir

Enterovirus replication: go with the (counter)flow
Jules Nchoutmboube, Lauren A. Ford-Siltz, George A. Belov

Revisiting phage therapy: new applications for old resources
Franklin L. Nobrega, Ana Rita Costa, Leon D. Kluskens, Joana Azeredo

Towards an HIV-1 cure: measuring the latent reservoir
Katherine M. Bruner, Nina N. Hosmane, Robert F. Siliciano

Virological features associated with the development of broadly neutralizing antibodies to HIV-1
Penny L. Moore, Carolyn Williamson, Lynn Morris

HIV-1 adaptation to HLA: a window into virus–host immune interactions
Jonathan M. Carlson, Anh Q. Le, Aniqa Shahid, Zabrina L. Brumme

Harnessing CRISPR–Cas systems for bacterial genome editing
Kurt Selle, Rodolphe Barrangou
Innovative techniques, sensors, and approaches for imaging biofilms at different scales
Thomas R. Neu, John R. Lawrence

Special Issue: Microbial Translocation

A fantastic voyage for sliding bacteria
Joshua D. Shrout

Positioning of bacterial chemoreceptors
Christopher W. Jones, Judith P. Armitage

Signaling and sensory adaptation in Escherichia coli chemoreceptors: 2015 update
John S. Parkinson, Gerald L. Hazelbauer, Joseph J. Falke

The bacterial flagellar motor and its structural diversity
Tohru Minamino, Katsumi Imada

The role of flagella in Clostridium difficile pathogenicity
Emma Stevenson, Nigel P. Minton, Sarah A. Kuehne

Axonal spread of neuroinvasive viral infections
Matthew P. Taylor, Lynn W. Enquist

HIV cell-to-cell transmission: effects on pathogenesis and antiretroviral therapy
Luis M. Agosto, Pradeep D. Uchil, Walther Mothes

Fueling type III secretion
Pei-Chung Lee, Arne Rietsch

Structural biology of the Gram-negative bacterial conjugation systems
Aravindan Ilangovan, Sarah Connery, Gabriel Waksman

Assembly and operation of bacterial tripartite multidrug efflux pumps
Dijun Du, Hendrik W. van Veen, Ben F. Luisi

Volume 23, Issue 6, June 2015

Detecting virulence and drug-resistance mycobacterial phenotypes in vivo
Graham S. Timmins

Hepatitis C virus screening to reveal a better picture of infection
Maria Cristina Medici, Claudio Galli, Adriana Calderaro

AI-2 to the rescue against antibiotic-induced intestinal dysbiosis?
Zhongke Sun, Verena Grimm, Christian U. Riedel

Novel role of DNA in neutrophil extracellular traps
Christoph Georg Baums, Maren von Köckritz-Blickwede

Gut bacteria and necrotizing enterocolitis: cause or effect?
Christopher James Stewart, Stephen Paul Cummings

Temporal patterns of rarity provide a more complete view of microbial diversity
Ashley Shade, Jack A. Gilbert
Are nematodes a missing link in the confounded ecology of the entomopathogen Bacillus thuringiensis?
Lifang Ruan, Neil Crickmore, Donghai Peng, Ming Sun

The essential features and modes of bacterial polar growth
Todd A. Cameron, John R. Zupan, Patricia C. Zambrayski

Fate, activity, and impact of ingested bacteria within the human gut microbiota
Muriel Derrien, Johan E.T. van Hylckama Vlieg

Does chronic infection in retroviruses have a sense?
Benoit Barbeau, Jean-Michel Mesnard

Sticky microbes: forces in microbial cell adhesion
Yves F. Dufrêne

Volume 23, Issue 7, July 2015

Getting to the root of epidemic spread with phylodynamic analysis of genomic data
Louis du Plessis, Tanja Stadler

How Ebola has been evolving in West Africa
Si-Qing Liu, Simon Rayner, Bo Zhang

Infectious asthma triggers: time to revise the hygiene hypothesis?
Wilmore C. Webley, Kelly L. Aldridge

Emerging intracellular receptors for hemorrhagic fever viruses
Lucas T. Jae, Thijn R. Brummelkamp

Collateral sensitivity of antibiotic-resistant microbes
Csaba Pal, Balazs Papp, Viktoria Lazar

The changing face of asthma and its relation with microbes
Chris S. Earl, Shi-qi An, Robert P. Ryan

Resistance is not futile: gliotoxin biosynthesis, functionality and utility
Stephen K. Dolan, Grainne O’Keeffe, Gary W. Jones, Sean Doyle

Improving preclinical models of HIV microbicide efficacy
Nadia R. Roan, Jan Münch

Multipurpose prevention technologies: the future of HIV and STI protection
José A. Fernández-Romero, Carolyn Deal, Betsy C. Herold, John Schiller, Dorothy Patton, Thomas Zydowsky, Joe Romano, Christopher D. Petro, Manjulaa Narasimhan

Staphylococcus aureus infections: transmission within households and the community
Justin Knox, Anne-Catrin Uhlemann, Franklin D. Lowy
Lokiarchaeota: eukaryote-like missing links from microbial dark matter?  
Arshan Nasir, Kyung Mo Kim, Gustavo Caetano-Anolles  

The giant panda gut microbiome  
Fuwen Wei, Xiao Wang, Qi Wu  

Entry and exit of bacterial outer membrane proteins  
Rajeev Misra  

Is Campylobacter to esophageal adenocarcinoma as Helicobacter is to gastric adenocarcinoma?  
Nadeem O. Kaakoush, Natalia Castaño-Rodríguez, Si Ming Man, Hazel M. Mitchell  

Evolution of bacterial transcription factors: how proteins take on new tasks, but do not always stop doing the old ones  
Sandhya S. Visweswariah, Stephen J.W. Busby  

Bat-to-human: spike features determining ‘host jump’ of coronaviruses SARS-CoV, MERS-CoV, and beyond  
Guangwen Lu, Qihui Wang, George F. Gao  

Whole-genome sequence comparisons reveal the evolution of Vibrio cholerae O1  
Eun Jin Kim, Chan Hee Lee, G. Balakrish Nair, Dong Wook Kim  

Nitrogen cycling in corals: the key to understanding holobiont functioning?  
Nils Rädecker, Claudia Pogoreutz, Christian R. Voolstra, Jörg Wiedenmann, Christian Wild  

Tackling antimicrobial resistance at global and local scales  
Hellen Gelband, Ramanan Laxminarayan  

Tolerance engineering in bacteria for the production of advanced biofuels and chemicals  
Aindrila Mukhopadhyay  

RNA structures are involved in the thermoregulation of bacterial virulence-associated traits  
María Victoria Grosso-Becera, Luis Servín-González, Gloria Soberón-Chávez  

Languages and dialects: bacterial communication beyond homoserine lactones  
Sophie Brameyer, Helge B. Bode, Ralf Heermann  

Targeting specific bacteria in the oral microbiome  
Jorge Frias-Lopez  

Complex host genetic susceptibility to Staphylococcus aureus infections  
Sanjay K. Shukla, Warren Rose, Steven J. Schrodi  

The potential impact of coinfection on antimicrobial chemotherapy and drug resistance  
Ruthie B. Birger, Roger D. Koupes, Ted Cohen, Emily C. Griffiths, Silvie Huijben, Michael J. Mina, Victoriya Volkova, Bryan Grenfell, C. Jessica E. Metcalf  

Bacterial cellulose biosynthesis: diversity of operons, subunits, products, and functions
Valerie Le Sage, Alessandro Cinti, Andrew J. Mouland

Rerouting Resistance: Escaping Restriction Using Alternative Cellular Pathways
Ailie Marx, Akram Alian

Rates of Lateral Gene Transfer in Prokaryotes: High but Why?
Michiel Vos, Matthijn C. Hesselman, Tim A. te Beek, Mark W.J. van Passel, Adam Eyre-Walker

Engineering Microbiomes to Improve Plant and Animal Health
U.G. Mueller, J.L. Sachs

Roles of Lipoproteins and Apolipoproteins in Particle Formation of Hepatitis C Virus
Takasuke Fukuhara, Chikako Ono, Francesc Puig-Basagoiti, Yoshiharu Matsuura

Sweet Talk: Protein Glycosylation in Bacterial Interaction With the Host
Qiuhe Lu, Shan Li, Feng Shao

Natural Product Biosynthetic Diversity and Comparative Genomics of the Cyanobacteria
Elke Dittmann, Muriel Gugger, Kaarina Sivonen, David P. Fewer

Antiviral Monoclonal Antibodies: Can They Be More Than Simple Neutralizing Agents?
Mireia Pelegrin, Mar Naranjo-Gomez, Marc Piechaczyk

Volume 23, Issue 11, November 2015

Biofilm Recruitment of Vibrio cholerae by Matrix Proteolysis
Marylise Duperthuy, Bernt Eric Uhlin, Sun Nyunt Wai

One of These is Not Like the Others
Martin S. Pavelka Jr

Microbial Malaise: How Can We Classify the Microbiome?
Robert G. Beiko

SAMHD1: At the Crossroads of Cell Proliferation, Immune Responses, and Virus Restriction
Ester Ballana, José A. Esté

Bacterial Amyloid Formation: Structural Insights into Curli Biogenesis
Nani Van Gerven, Roger D. Klein, Scott J. Hultgren, Han Remaut

Roles of Indole as an Interspecies and Interkingdom Signaling Molecule
Jin-Hyung Lee, Thomas K. Wood, Jintae Lee

Microbial Invasions: The Process, Patterns, and Mechanisms
Cyrus Alexander Mallon, Jan Dirk van Elsas, Joana Falcão Salles

Ten Years of Maintaining and Expanding a Microbial Genome and Metagenome Analysis System
Victor M. Markowitz, I-Min A. Chen, Ken Chu, Amrita Pati, Natalia N. Ivanova, Nikos C. Kyrpides
Programming Bacteriophages by Swapping Their Specificity Determinants
Moran G. Goren, Ido Yosef, Udi Qimron

Small Molecules Take A Big Step Against Clostridium difficile
Greg L. Beilhartz, John Tam, Roman A. Melnyk

Adipose Tissue: Sanctuary for HIV/SIV Persistence and Replication
Suresh Pallikkuth, Mahesh Mohan

The Mineralosphere Concept: Mineralogical Control of the Distribution and Function of Mineral-associated Bacterial Communities
Stephane Uroz, Laura Catherine Kelly, Marie-Pierre Turpault, Cendrella Lepleux, Pascale Frey-Klett

The HIV-1 Entry Process: A Stoichiometric View
Oliver F. Brandenberg, Carsten Magnus, Roland R. Regoes, Alexandra Trkola

How Bacteria Use Type IV Pili Machinery on Surfaces
Berenike Maier, Gerard C.L. Wong

Stealing the Keys to the Kitchen: Viral Manipulation of the Host Cell Metabolic Network
Christopher M. Goodwin, Shihao Xu, Joshua Munger

Pentraxins and Collectins: Friend or Foe during Pathogen Invasion?
Suan-Sin Foo, Patrick C. Reading, Sébastien Jaillon, Alberto Mantovani, Suresh Mahalingam

Brucella abortus Cell Cycle and Infection Are Coordinated
Xavier De Bolle, Sean Crosson, Jean-Yves Matroule, Jean-Jacques Letesson
Volume 23, Issue 1, January 2015

On the early dynamics and spread of HIV-1
Brittany Rife, Marco Salemi

Abstract
Until recently, the origin of the HIV-1 group M pandemic largely remained a scientific mystery. The use of comprehensive evolutionary analyses has revealed a unique story regarding viral migration, starting in the 1920s in Kinshasa, and the social and infrastructural changes associated with the early spread of this deadly virus.

Cell-size maintenance: universal strategy revealed
Suckjoon Jun, Sattar Taheri-Araghi

Abstract
How cells maintain a stable size has fascinated scientists since the beginning of modern biology, but has remained largely mysterious. Recently, however, the ability to analyze single bacteria in real time has provided new, important quantitative insights into this long-standing question in cell biology.

Bridging the gap between viable but non-culturable and antibiotic persistent bacteria
Mesrop Ayrapetyan, Tiffany C. Williams, James D. Oliver

Abstract
Microbial dormancy is a widespread phenomenon employed by bacteria to evade environmental threats including antibiotics. This intrinsic mechanism of antibiotic tolerance has drawn special attention to the role of dormancy in human disease, particularly in regards to recurrent infections. Two dormancy states, the viable but non-culturable state and bacterial persistence, both produce antibiotic-tolerant populations capable of withstanding prolonged lethal treatment. Currently described as two distinct forms of dormancy, they are rarely discussed in the same context. We argue here that these two dormant states are closely related phenomena which are part of a shared ‘dormancy continuum’. This discussion is intended to stimulate discourse about these seemingly different but very similar dormant states.

Diversity and disease pathogenesis in Mycobacterium tuberculosis
Digby F. Warner, Anastasia Koch, Valerie Mizrahi

Abstract
The increasing availability of whole-genome sequence (WGS) data for Mycobacterium tuberculosis, the bacterium that causes tuberculosis (TB), suggests that circulating genotypes have been molded by three dominant evolutionary forces: long-term persistence within the human population, which requires a core programme of infection, disease, and transmission; selective pressure on specific genomic loci, which provides evidence of lineage-specific adaptation to host populations; and drug exposure, which has driven the rapid emergence of resistant isolates following the global implementation of anti-TB chemotherapy. Here, we provide an overview of these factors in considering the implications of genotypic diversity for disease pathogenesis, vaccine efficacy, and drug treatment.
**Bacterial microcompartments and the modular construction of microbial metabolism**
Cheryl A. Kerfeld, Onur Erbilgin

**Abstract**

Bacterial microcompartments (BMCs) are protein-bound organelles predicted to be present across 23 bacterial phyla. BMCs facilitate carbon fixation as well as the aerobic and anaerobic catabolism of a variety of organic compounds. These functions have been linked to ecological nutrient cycling, symbiosis, pathogenesis, and cardiovascular disease. Within bacterial cells, BMCs are metabolic modules that can be further dissociated into their constituent structural and functional protein domains. Viewing BMCs as genetic, structural, functional, and evolutionary modules provides a framework for understanding both BMC-mediated metabolism and for adapting their architectures for applications in synthetic biology.

**Arthritogenic alphaviruses: new insights into arthritis and bone pathology**
Weiqiang Chen, Suan-Sin Foo, Natalie A. Sims, Lara J. Herrero, Nicole C. Walsh, Suresh Mahalingam

**Abstract**

Arthritogenic alphaviral infection begins as a febrile illness and often progresses to joint pain and rheumatic symptoms that are described as polyarthritis. Alphaviral arthritis and classical arthritides share many similar cellular and immune mediators involved in their pathogenesis. Recent *in vitro* and *in vivo* evidence suggests that bone loss resulting from increased expression of bone resorption mediators may accompany alphaviral infection. In addition, several longitudinal studies have reported more severe and delayed recovery of alphaviral disease in patients with pre-existing arthritic conditions. This review aims to provide insights into alphavirus-induced bone loss and focuses on aspects of disease exacerbation in patients with underlying arthritis and on possible therapeutic targets.

**Multidrug resistance genes in staphylococci from animals that confer resistance to critically and highly important antimicrobial agents in human medicine**
Sarah Wendlandt, Jianzhong Shen, Kristina Kadlec, Yang Wang, Beibei Li, Wan-Jiang Zhang, Andrea T. Feßler, Congming Wu, Stefan Schwarz

**Abstract**

Most antimicrobial resistance genes known so far to occur in staphylococci of animal origin confer resistance to a specific class of antimicrobial agents or to selected members within such a class. However, there are also a few examples of multidrug resistance (MDR) genes that confer resistance to antimicrobial agents of different classes by either target site methylation or active efflux via ATP-binding cassette (ABC) transporters. The present review provides an overview of these MDR genes with particular reference to those genes involved in resistance to critically or highly important antimicrobial agents used in human and veterinary medicine. Moreover, their location on mobile genetic elements and colocated resistance genes, which may play a role in coselection and persistence of the MDR genes, are addressed.
**Response of host inflammasomes to viral infection**
I-Yin Chen, Takeshi Ichinohe

**Abstract**

Inflammasomes are multiprotein complexes that induce downstream immune responses to specific pathogens, environmental stimuli, and host cell damage. Components of specific viruses activate different inflammasomes; for example, the influenza A virus M2 protein and encephalomyocarditis virus (EMCV) 2B protein activate the nucleotide-binding oligomerization domain (NOD)-like receptor family pyrin domain (PYD)-containing 3 (NLRP3) inflammasome, whereas viral double-stranded RNA (dsRNA) activates the retinoic acid inducible gene-I (RIG-I) inflammasome. Once activated in response to viral infection, inflammasomes induce the activation of caspases and the release of mature forms of interleukin-1β (IL-1β) and IL-18. Here we review the association between viral infection and inflammasome activation. Identifying the mechanisms underlying virus-induced inflammasome activation is important if we are to develop novel therapeutic strategies to target viruses.

**Volume 23, Issue 2, Pages 65-120 (February 2015)**

**A race for an Ebola vaccine: promises and obstacles**

**Abstract**

While several impeding factors have limited Ebola vaccine development, the current epidemic has provided a surge which may lead to a record pace for a vaccine against Ebola. Consequently, multiple FDA trials are currently underway using two promising vaccine platforms; one has recently demonstrated durable immunity within non-human primates.

**Success in incorporating horizontally transferred genes: the H-NS protein**
Mario Hütten, Sonia Paytubi, Antonio Juárez

**Abstract**

The nucleoid-associated protein H-NS silences unwanted expression of acquired foreign DNA. Ali and colleagues recently identified which horizontally-acquired genes are targeted by H-NS in *Salmonella* to avoid fitness loss. The reported data strengthen our view about the role of H-NS in bacterial evolution driven by horizontal gene transfer.

**Transmission of antimicrobial resistance in resource-poor healthcare**
Jodi A. Lindsay

**Abstract**

Inter-patient transfer of antimicrobial resistant pathogens is more common in resource-poor healthcare settings. In this age of global resistance, what contributes to the spread of antimicrobial resistant clones?

**Solving the etiology of dental caries**
Aurea Simón-Soro, Alex Mira

**Abstract**

For decades, the sugar-fermenting, acidogenic species *Streptococcus mutans* has been considered the main causative agent of dental caries and most diagnostic and therapeutic strategies have been targeted toward this microorganism. However, recent DNA- and RNA-based studies from carious lesions have uncovered an extraordinarily diverse ecosystem where *S. mutans* accounts only a tiny fraction of the bacterial community. This supports the concept that consortia formed by multiple microorganisms act collectively, probably synergistically, to initiate and expand the cavity. Thus, antimicrobial therapies are not expected to be effective in the treatment of caries and other polymicrobial diseases that do not follow classical Koch's postulates.
Elite control of HIV: is this the right model for a functional cure?
Leslie R. Cockerham, Hiroyu Hatano

Abstract

A cure for HIV is still greatly needed and has become a global research priority. A unique subset of HIV-infected individuals who spontaneously control HIV exists, and these are known as ‘elite controllers’. They may represent a natural model for a ‘functional cure’ in which there is long term control of viral replication and remission from symptoms of HIV infection in the absence of antiretroviral therapy. However, controllers have evidence of ongoing inflammation, CD4+ T cell depletion, and perhaps even inflammation-associated cardiovascular disease, suggesting that this natural long term virologic control may be coming at an immunologic and clinical cost. These individuals may continue to provide continued insights into mechanisms of host control; however, they may not represent the best model of a functional cure, if we believe that a cure should require a disease-free (and not just a treatment-free) state.

Viral biocontrol: grand experiments in disease emergence and evolution
Francesca Di Giallonardo, Edward C. Holmes

Abstract

Although viral emergence is commonly associated with cross-species transmission, the processes and determinants of viral evolution in a novel host environment are poorly understood. We address key questions in virus emergence and evolution using data generated from two unique natural experiments: the deliberate release of myxoma virus (MYXV) and rabbit hemorrhagic disease virus (RHDV) as biological control (biocontrol) agents against the European rabbit in Australia, and which have been of enormous benefit to Australia's ecosystem and agricultural industries. Notably, although virulence evolution in MYXV and RHDV followed different trajectories, a strongly parallel evolutionary process was observed in Australia and Europe. These biocontrol agents were also characterized by a lack of transmission to nontarget host species, suggesting that there are major barriers to successful emergence.

Light-driven ion-translocating rhodopsins in marine bacteria
Keiichi Inoue, Yoshitaka Kato, Hideki Kandori

Abstract

Microbial rhodopsins are the photoreceptive membrane proteins found in diverse microorganisms from within Archaea, Eubacteria, and eukaryotes. They have a heptahelical transmembrane structure that binds to an all-trans retinal chromophore. Since 2000, thousands of proteorhodopsins, genes of light-driven proton pump rhodopsins, have been identified from various species of marine bacteria. This suggests that they are used for the conversion of light into chemical energy, contributing to carbon circulation related to ATP synthesis in the ocean. Furthermore, novel types of rhodopsin (sodium and chloride pumps) have recently been discovered. Here, we review recent progress in our understanding of ion-transporting rhodopsins of marine bacteria, based mainly on biophysical and biochemical research.
Understanding carbon catabolite repression in Escherichia coli using quantitative models
A. Kremling, J. Geiselmann, D. Ropers, H. de Jong

Abstract

Carbon catabolite repression (CCR) controls the order in which different carbon sources are metabolized. Although this system is one of the paradigms of the regulation of gene expression in bacteria, the underlying mechanisms remain controversial. CCR involves the coordination of different subsystems of the cell that are responsible for the uptake of carbon sources, their breakdown for the production of energy and precursors, and the conversion of the latter to biomass. The complexity of this integrated system, with regulatory mechanisms cutting across metabolism, gene expression, and signaling, and that are subject to global physical and physiological constraints, has motivated important modeling efforts over the past four decades, especially in the enterobacterium Escherichia coli. Different hypotheses concerning the dynamic functioning of the system have been explored by a variety of modeling approaches. We review these studies and summarize their contributions to the quantitative understanding of CCR, focusing on diauxic growth in E. coli. Moreover, we propose a highly simplified representation of diauxic growth that makes it possible to bring out the salient features of the models proposed in the literature and confront and compare the explanations they provide.

Nucleoside antibiotics: biosynthesis, regulation, and biotechnology
Guoqing Niu, Huarong Tan

Abstract

The alarming rise in antibiotic-resistant pathogens has coincided with a decline in the supply of new antibiotics. It is therefore of great importance to find and create new antibiotics. Nucleoside antibiotics are a large family of natural products with diverse biological functions. Their biosynthesis is a complex process through multistep enzymatic reactions and is subject to hierarchical regulation. Genetic and biochemical studies of the biosynthetic machinery have provided the basis for pathway engineering and combinatorial biosynthesis to create new or hybrid nucleoside antibiotics. Dissection of regulatory mechanisms is leading to strategies to increase the titer of bioactive nucleoside antibiotics.

Volume 23, Issue 3, March 2015

Following the equator: division site selection in Streptococcus pneumoniae
Marc Bramkamp

Abstract

The mechanisms that spatially regulate cytokinesis are more diverse than initially thought. In two recent publications a positive regulator of FtsZ positioning has been identified in Streptococcus pneumoniae. MapZ (LocZ) connects the division machinery with cell wall elongation, providing a simple mechanism to ensure correct division site selection.

Architectural plan of transcriptional regulation in Mycobacterium tuberculosis
Priyanka Baloni, Nagasuma Chandra

Abstract

Transcriptional regulation enables adaptation in bacteria. Typically, only a few transcriptional events are well understood, leaving many others unidentified. The recent genome-wide identification of transcription factor binding sites in Mycobacterium tuberculosis has changed this by deciphering a molecular road-map of transcriptional control, indicating active events and their immediate downstream effects.
Is selection relevant in the evolutionary emergence of drug resistance?
Troy Day, Silvie Huijben, Andrew F. Read

Abstract

The emergence of drug-resistant pathogens is often considered a canonical case of evolution by natural selection. Here we argue that the strength of selection can be a poor predictor of the rate of resistance emergence. It is possible for a resistant strain to be under negative selection and still emerge in an infection or spread in a population. Measuring the right parameters is a necessary first step toward the development of evidence-based resistance-management strategies. We argue that it is the absolute fitness of the resistant strains that matters most and that a primary determinant of the absolute fitness of a resistant strain is the ecological context in which it finds itself.

The demographic determinants of human microbiome health
Sylvie Estrela, Marvin Whiteley, Sam P. Brown

Abstract

The human microbiome is a vast reservoir of microbial diversity and increasingly recognized to have a fundamental role in human health. In polymicrobial communities, the presence of one species can modulate the demography (i.e., growth and distribution) of other species. These demographic impacts generate feedbacks in multispecies interactions, which can be magnified in spatially structured populations (e.g., host-associated communities). Here, we argue that demographic feedbacks between species are central to microbiome development, shaping whether and how potential metabolic interactions come to be realized between expanding lineages of bacteria. Understanding how demographic feedbacks tune metabolic interactions and in turn shape microbiome structure and function is now a key challenge to our abilities to better manage microbiome health.

Reverse zoonosis of influenza to swine: new perspectives on the human–animal interface
Martha I. Nelson, Amy L. Vincent

Abstract

The origins of the 2009 influenza A (H1N1) pandemic in swine are unknown, highlighting gaps in our understanding of influenza A virus (IAV) ecology and evolution. We review how recently strengthened influenza virus surveillance in pigs has revealed that influenza virus transmission from humans to swine is far more frequent than swine-to-human zoonosis, and is central in seeding swine globally with new viral diversity. The scale of global human-to-swine transmission represents the largest ‘reverse zoonosis’ of a pathogen documented to date. Overcoming the bias towards perceiving swine as sources of human viruses, rather than recipients, is key to understanding how the bidirectional nature of the human–animal interface produces influenza threats to both hosts.

Mx GTPases: dynamin-like antiviral machines of innate immunity
Otto Haller, Peter Staehehi, Martin Schwemmle, Georg Kochs

Abstract

The Mx dynamin-like GTPases are key antiviral effector proteins of the type I and type III interferon (IFN) systems. They inhibit several different viruses by blocking early steps of the viral replication cycle. We focus on new structural and functional insights and discuss recent data revealing that human MxA (MX1) provides a safeguard against introduction of avian influenza A viruses (FLUAV) into the human population. The related human MxB (MX2) serves as restriction factor for HIV-1 and other primate lentiviruses.
The general stress response in Alphaproteobacteria
Anne Francez-Charlot, Andreas Kaczmarszyk, Hans-Martin Fischer, Julia A. Vorholt

Abstract

The general stress response (GSR) is a widely conserved response that allows bacteria to cope with a multitude of stressful conditions. In the past years the PhyR–NepR–σEcfG cascade was identified as the core pathway regulating the GSR in Alphaproteobacteria, in which it also plays an important role in bacteria–host interactions. The regulatory system is composed of the extracytoplasmic function sigma factor σEcfG, its anti-sigma factor NepR (for negative regulator of the PhyR response), and the anti-sigma factor antagonist PhyR (phyllosphere regulator). The three proteins function via a partner-switching mechanism that is triggered by PhyR phosphorylation, termed ‘sigma factor mimicry’. This review will cover core features of the pathway, its physiological role, and summarize recent advances towards understanding of the partner-switching mechanism and of the two-component signaling pathways controlling the GSR.

Bats as ‘special’ reservoirs for emerging zoonotic pathogens
Cara E. Brook, Andrew P. Dobson

Abstract

The ongoing West African Ebola epidemic highlights a recurring trend in the zoonotic emergence of virulent pathogens likely to come from bat reservoirs that has caused epidemiologists to ask ‘Are bats special reservoirs for emerging zoonotic pathogens?’ We collate evidence from the past decade to delineate mitochondrial mechanisms of bat physiology that have evolved to mitigate oxidative stress incurred during metabolically costly activities such as flight. We further describe how such mechanisms might have generated pleiotropic effects responsible for tumor mitigation and pathogen control in bat hosts. These synergisms may enable ‘special’ tolerance of intracellular pathogens in bat hosts; paradoxically, this may leave them more susceptible to immunopathological morbidity when attempting to clear extracellular infections such as ‘white-nose syndrome’ (WNS).

Volume 23, Issue 4, April 2015

Meningitis in adolescents: the role of commensal microbiota
James W.B. Moir

Abstract

The pathogen Neisseria meningitidis causes disease amongst infants and adolescents/young adults. Here we argue that disease amongst adolescents is due largely to interaction between N. meningitidis and other members of the upper respiratory tract microbiota, through a metabolic interaction involving exchange of propionic acid.

Enterovirus replication: go with the (counter)flow
Jules Nchoutmboube, Lauren A. Ford-Siltz, George A. Belov

Abstract

All (+)RNA viruses replicate on distinct membranous domains; however, how they induce and maintain their unique lipid composition is largely unknown. Two recent studies reveal that enteroviruses harness the PI4P–cholesterol exchange cycle driven by OSBP1 protein and PI4 kinase(s), and that blocking the dynamic lipid flow inhibits virus replication.
Revisiting phage therapy: new applications for old resources
Franklin L. Nobrega, Ana Rita Costa, Leon D. Kluskens, Joana Azeredo

Abstract

The success of phage therapy is dependent on the development of strategies able to overcome the limitations of bacteriophages as therapeutic agents, the creation of an adequate regulatory framework, the implementation of safety protocols, and acceptance by the general public. Many approaches have been proposed to circumvent phages’ intrinsic limitations but none have proved to be completely satisfactory. In this review we present the major hurdles of phage therapy and the solutions proposed to circumvent them. A thorough discussion of the advantages and drawbacks of these solutions is provided and special attention is given to the genetic modification of phages as an achievable strategy to shape bacteriophages to exhibit desirable biological properties.

Towards an HIV-1 cure: measuring the latent reservoir
Katherine M. Bruner, Nina N. Hosmane, Robert F. Siliciano

Abstract

The latent reservoir (LR) of HIV-1 in resting memory CD4+ T cells serves as a major barrier to curing HIV-1 infection. While many PCR- and culture-based assays have been used to measure the size of the LR, correlation between results of different assays is poor and recent studies indicate that no available assay provides an accurate measurement of reservoir size. The discrepancies between assays are a hurdle to clinical trials that aim to measure the efficacy of HIV-1 eradication strategies. Here we describe the advantages and disadvantages of various approaches to measuring the LR.

Virological features associated with the development of broadly neutralizing antibodies to HIV-1
Penny L. Moore, Carolyn Williamson, Lynn Morris

Abstract

The development of a preventative HIV-1 vaccine remains a global public health priority. This will likely require the elicitation of broadly neutralizing antibodies (bNAb) able to block infection by diverse viral strains from across the world. Understanding the pathway to neutralization breadth in HIV-1 infected humans will provide insights into how bNAAb lineages arise, a process that probably involves a combination of host and viral factors. Here, we focus on the role of viral characteristics and evolution in shaping bNAb during HIV-1 infection, and describe how these findings may be translated into novel vaccine strategies.

HIV-1 adaptation to HLA: a window into virus–host immune interactions
Jonathan M. Carlson, Anh Q. Le, Aniqa Shahid, Zabrina L. Brumme

Abstract

HIV-1 develops specific mutations within its genome that allow it to escape detection by human leukocyte antigen (HLA) class I-restricted immune responses, notably those of CD8+ cytotoxic T lymphocytes (CTL). HLA thus represents a major force driving the evolution and diversification of HIV-1 within individuals and at the population level. Importantly, the study of HIV-1 adaptation to HLA also represents an opportunity to identify what qualities constitute an effective immune response, how the virus in turn adapts to these pressures, and how we may harness this information to design HIV-1 vaccines that stimulate effective cellular immunity.
Harnessing CRISPR–Cas systems for bacterial genome editing
Kurt Selle, Rodolphe Barrangou

Abstract
Manipulation of genomic sequences facilitates the identification and characterization of key genetic determinants in the investigation of biological processes. Genome editing via clustered regularly interspaced short palindromic repeats (CRISPR)–CRISPR-associated (Cas) constitutes a next-generation method for programmable and high-throughput functional genomics. CRISPR–Cas systems are readily reprogrammed to induce sequence-specific DNA breaks at target loci, resulting in fixed mutations via host-dependent DNA repair mechanisms. Although bacterial genome editing is a relatively unexplored and underrepresented application of CRISPR–Cas systems, recent studies provide valuable insights for the widespread future implementation of this technology. This review summarizes recent progress in bacterial genome editing and identifies fundamental genetic and phenotypic outcomes of CRISPR targeting in bacteria, in the context of tool development, genome homeostasis, and DNA repair.

Innovative techniques, sensors, and approaches for imaging biofilms at different scales
Thomas R. Neu, John R. Lawrence

Abstract
Confocal laser scanning microscopy has become a standard technique for the investigation of hydrated interfacial microbial communities at the microscale. Multiphoton and spinning-disk microscopes provide new options for in situ imaging. Progress has been made in imaging structural aspects as well as interactions and processes. Advanced fluorescence techniques such as lifetime imaging and correlation spectroscopy are also available. Newly developed target-specific probes allow investigation of new aspects of microbial communities. Several new laser-based techniques are available including nanoscopy and mesoscale techniques. Nanoscopy techniques offer access to unprecedented resolution of hydrated microbiological samples at the scale of fluorescent gene products and macromolecules. Mesoscale approaches are important to address larger features and statistical issues of microbiological samples. This review presents the state of the art in situ biofilm imaging and assesses the pros and cons of laser-based imaging techniques in combination with a variety of sensor types at different scales.

Special Issue: Microbial Translocation

A fantastic voyage for sliding bacteria
Joshua D. Shrout

Abstract
A recent study showed that Salmonella enterica serovar Typhimurium exhibits sliding motility under magnesium-limited conditions. Overall, bacteria that exhibit this passive surface movement described as sliding share few common traits. This discovery provides an opportunity to revisit and better characterize appendage-independent bacterial motility.
Positioning of bacterial chemoreceptors
Christopher W. Jones, Judith P. Armitage

Abstract

For optimum growth, bacteria must adapt to their environment, and one way that many species do this is by moving towards favourable conditions. To do so requires mechanisms to both physically drive movement and provide directionality to this movement. The pathways that control this directionality comprise chemoreceptors, which, along with an adaptor protein (CheW) and kinase (CheA), form large hexagonal arrays. These arrays can be formed around transmembrane receptors, resulting in arrays embedded in the inner membrane, or they can comprise soluble receptors, forming arrays in the cytoplasm. Across bacterial species, chemoreceptor arrays (both transmembrane and soluble) are localised to a variety of positions within the cell; some species with multiple arrays demonstrate this variety within individual cells. In many cases, the positioning pattern of the arrays is linked to the need for segregation of arrays between daughter cells on division, ensuring the production of chemotactically competent progeny. Multiple mechanisms have evolved to drive this segregation, including stochastic self-assembly, cellular landmarks, and the utilisation of ParA homologues. The variety of mechanisms highlights the importance of chemotaxis to motile species.

Signaling and sensory adaptation in Escherichia coli chemoreceptors: 2015 update
John S. Parkinson, Gerald L. Hazelbauer, Joseph J. Falke

Abstract

Motile Escherichia coli cells track gradients of attractant and repellent chemicals in their environment with transmembrane chemoreceptor proteins. These receptors operate in cooperative arrays to produce large changes in the activity of a signaling kinase, CheA, in response to small changes in chemoeffector concentration. Recent research has provided a much deeper understanding of the structure and function of core receptor signaling complexes and the architecture of higher-order receptor arrays, which, in turn, has led to new insights into the molecular signaling mechanisms of chemoreceptor networks. Current evidence supports a new view of receptor signaling in which stimulus information travels within receptor molecules through shifts in the dynamic properties of adjoining structural elements rather than through a few discrete conformational states.

The bacterial flagellar motor and its structural diversity
Tohru Minamino, Katsumi Imada

Abstract

The bacterial flagellum is a reversible rotary motor powered by an electrochemical-potential difference of specific ions across the cytoplasmic membrane. The H⁺-driven motor of Salmonella spins at ~300 Hz, whereas the Na⁺-driven motor of marine Vibrio spp. can rotate much faster, up to 1700 Hz. A highly conserved motor structure consists of the MS ring, C ring, rod, and export apparatus. The C ring and the export apparatus show dynamic properties for exerting their functional activities. Various additional structures surrounding the conserved motor structure are observed in different bacterial species. In this review we summarize our current understanding of the structure, function, and assembly of the flagellar motor in Salmonella and marine Vibrio.
The role of flagella in Clostridium difficile pathogenicity
Emma Stevenson, Nigel P. Minton, Sarah A. Kuehne

Abstract
Clostridium difficile is widely publicised as a problem in the health-care system. Disruption of the normal gut microbiota by antibiotic therapy allows C. difficile to colonise the colon. On colonisation, C. difficile produces two toxins that lead to disease, with symptoms ranging from mild-to-severe diarrhoea, to fulminant and often fatal pseudomembranous colitis (PMC). How C. difficile establishes initial colonisation of the host is an area of active investigation. Recently there has been increased research into the role of C. difficile flagella in colonisation and adherence. Novel research has also elucidated a more complex role of flagella in C. difficile virulence pertaining to the regulation of toxin gene expression. This review focuses on new insights into the specific role of C. difficile flagella in colonisation and toxin gene expression.

Axonal spread of neuroinvasive viral infections
Matthew P. Taylor, Lynn W. Enquist

Abstract
Neuroinvasive viral infections invade the nervous system, often eliciting serious disease and death. Members of four viral families are both neuroinvasive and capable of transmitting progeny virions or virion components within the long neuronal extensions known as axons. Axons provide physical structures that enable viral infection to spread within the host while avoiding extracellular immune responses. Technological advances in the analysis of in vivo neural circuits, neuronal culturing, and live imaging of fluorescent fusion proteins have enabled an unprecedented view into the steps of virion assembly, transport, and egress involved in axonal spread. In this review we summarize the literature supporting anterograde (axon to cell) spread of viral infection, describe the various strategies of virion transport, and discuss the effects of spread on populations of neuroinvasive viruses.

HIV cell-to-cell transmission: effects on pathogenesis and antiretroviral therapy
Luis M. Agosto, Pradeep D. Uchil, Walther Mothes

Abstract
HIV spreads more efficiently in vitro when infected cells directly contact uninfected cells to form virological synapses. A hallmark of virological synapses is that viruses can be transmitted at a higher multiplicity of infection (MOI) that, in vitro, results in a higher number of proviruses. Whether HIV also spreads by cell–cell contact in vivo is a matter of debate. Here we discuss recent data that suggest that contact-mediated transmission largely manifests itself in vivo as CD4+ T cell depletion. The assault of a cell by a large number of incoming particles is likely to be efficiently sensed by the innate cellular surveillance to trigger cell death. The large number of particles transferred across virological synapses has also been implicated in reduced efficacy of antiretroviral therapies. Thus, antiretroviral therapies must remain effective against the high MOI observed during cell-to-cell transmission to inhibit both viral replication and the pathogenesis associated with HIV infection.

Fueling type III secretion
Pei-Chung Lee, Arne Rietsch

Abstract
Type III secretion systems (T3SSs) are complex nanomachines that export proteins from the bacterial cytoplasm across the cell envelope in a single step. They are at the core of the machinery used to assemble the bacterial flagellum, and the needle complex many Gram-negative pathogens use to inject effector proteins into host cells and cause disease. Several models have been put forward to explain how this export is energized, and the mechanism has been the subject of considerable debate. Here we present an overview of these models and discuss their relative merits. Recent evidence suggests that the proton motive force (pmf) is the primary energy source for type III secretion, although contribution from refolding of secreted proteins has not been ruled out. The mechanism by which the pmf is converted to protein export remains enigmatic.
Structural biology of the Gram-negative bacterial conjugation systems
Aravindan Ilango van, Sarah Connery, Gabriel Waksman

Abstract

Conjugation, the process by which plasmid DNA is transferred from one bacterium to another, is mediated by type IV secretion systems (T4SSs). T4SSs are versatile systems that can transport not only DNA, but also toxins and effector proteins. Conjugative T4SSs comprise 12 proteins named VirB1–11 and VirD4 that assemble into a large membrane-spanning exporting machine. Before being transported, the DNA substrate is first processed on the cytoplasmic side by a complex called the relaxosome. The substrate is then targeted to the T4SS for export into a recipient cell. In this review, we describe the recent progress made in the structural biology of both the relaxosome and the T4SS.

Assembly and operation of bacterial tripartite multidrug efflux pumps
Dijun Du, Hendrik W. van Veen, Ben F. Luisi

Abstract

Microorganisms encode several classes of transmembrane pumps that can expel an enormous range of toxic substances, thereby improving their fitness in harsh environments and contributing to resistance against antimicrobial agents. In Gram-negative bacteria these pumps can take the form of tripartite assemblies that actively efflux drugs and other harmful compounds across the cell envelope. We describe recent structural and functional data that have provided insights into the transport mechanisms of these intricate molecular machines.

Volume 23, Issue 6, June 2015

Detecting virulence and drug-resistance mycobacterial phenotypes in vivo
Graham S. Timmins

Abstract

Bacterial phenotypes are predominantly studied in culture because detection of their specific metabolic pathways in the host is challenging. Development of stable-isotope breath tests, allowing in situ phenotype analyses, may endow diagnostics with new modalities based upon direct monitoring of in vivo microbial metabolism and host–pathogen phenotypic interactions.

Hepatitis C virus screening to reveal a better picture of infection
Maria Cristina Medici, Claudio Galli, Adriana Calderaro

Abstract

Antiviral therapy for hepatitis C virus (HCV) infection will be the next revolution in clinical virology. Sensible planning for treatment is needed, starting with population-screening policies ideally using the HCV core antigen. This will result in a more defined picture of the silent spread of HCV.

AI-2 to the rescue against antibiotic-induced intestinal dysbiosis?
Zhongke Sun, Verena Grimm, Christian U. Riedel

Abstract

The downside of antibiotic treatment of infectious diseases is a disturbed intestinal microbiota leading to reduced resistance against pathogen colonization. Work by Thompson et al. now suggests that antibiotic-induced intestinal dysbiosis can partially be counterbalanced by artificially increasing the levels of autoinducer-2 (AI-2), a well-known bacterial communication molecule.
**Novel role of DNA in neutrophil extracellular traps**
Christoph Georg Baums, Maren von Köckritz-Blickwede

**Abstract**

Neutrophil extracellular traps (NETs) have been shown to play a crucial role in health and disease. In a recent paper in *PLoS Pathogens*, Halverson et al. demonstrate that the DNA backbone of NETs contributes to its antibacterial activity and serves as signal for entrapped microbes to employ immune evasion strategies.

**Gut bacteria and necrotizing enterocolitis: cause or effect?**
Christopher James Stewart, Stephen Paul Cummings

**Abstract**

Development of necrotising enterocolitis (NEC) is considered to be dependent on the bacterial colonisation of the gut. With little concordance between published data and a recent study failing to detect a common strain in infants with NEC, more questions than answers are arising about our understanding of this complex disease.

**Temporal patterns of rarity provide a more complete view of microbial diversity**
Ashley Shade, Jack A. Gilbert

**Abstract**

Recently, conditionally rare taxa (CRTs) – those taxa that are typically in very low abundance but occasionally achieve prevalence – were shown to contribute to patterns of microbial diversity because their collective dynamics explained a large proportion of temporal variability in microbial community structure. Here the benefits and challenges of characterizing the presence and interpreting the role of CRTs are further explored, along with questions about CRT ecology. We also introduce a conceptual model for thinking about microbial taxa as dynamic components along the dimensions of occurrence and abundance. Accounting for CRTs in interpretations of microbial ecological dynamics is essential if we are to understand community stability and ecoevolutionary interactions.

**Are nematodes a missing link in the confounded ecology of the entomopathogen *Bacillus thuringiensis***?
Lifang Ruan, Neil Crickmore, Donghai Peng, Ming Sun

**Abstract**

*Bacillus thuringiensis*, which is well known as an entomopathogen, has been accepted by the public as a safe bioinsecticide. The natural ecology of this bacterium has never been particularly clear, with views ranging from it being an obligate pathogen to an opportunist pathogen that can otherwise exist as a soil saprophyte or a plant endophyte. This confusion has recently led to it being considered as an environmental pathogen that has evolved to occupy a diverse set of environmental niches in which it can thrive without needing a host. A significant driving force behind this classification is the fact that *B. thuringiensis* is found in high numbers in environments that are not occupied by the insect hosts to which it is pathogenic. It is our opinion that the ubiquitous presence of this bacterium in the environment is the result of a variety of vectoring systems, particularly those that include nematodes.
The essential features and modes of bacterial polar growth
Todd A. Cameron, John R. Zupan, Patricia C. Zambryski

Abstract

Polar growth represents a surprising departure from the canonical dispersed cell growth model. However, we know relatively little of the underlying mechanisms governing polar growth or the requisite suite of factors that direct polar growth. Underscoring how classic doctrine can be turned on its head, the peptidoglycan layer of polar-growing bacteria features unusual crosslinks and in some species the quintessential cell division proteins FtsA and FtsZ are recruited to the growing poles. Remarkably, numerous medically important pathogens utilize polar growth, accentuating the need for intensive research in this area. Here we review models of polar growth in bacteria based on recent research in the Actinomycetales and Rhizobiales, with emphasis on Mycobacterium and Agrobacterium species.

Fate, activity, and impact of ingested bacteria within the human gut microbiota
Muriel Derrien, Johan E.T. van Hylckama Vlieg

Abstract

The human gut contains a highly diverse microbial community that is essentially an open ecosystem, despite being deeply embedded within the human body. Food-associated fermentative bacteria, including probiotics, are major sources of ingested bacteria that may temporarily complement resident microbial communities, thus forming part of our transient microbiome. Here, we review data on the fate and activity of ingested bacteria and, in particular, lactobacilli and bifidobacteria in the gastrointestinal (GI) tract and their impact on the composition and metabolism of the gut microbiome with a focus on data from clinical studies. In addition, we discuss the mechanisms involved and the potential impact on the host's health.

Does chronic infection in retroviruses have a sense?
Benoit Barbeau, Jean-Michel Mesnard

Abstract

Over recent years, retroviral gene expression has been shown to depend on a promoter that is bidirectional. This promoter activity is likely to occur at either end of the retroviral genome and has important consequences at the level of retroviral gene expression. This review focuses on the recent discovery of retroviral antisense genes termed HBZ [in human T-cell leukemia virus type 1 (HTLV-1)] and ASP (in HIV-1) in terms of their function and the regulation of their expression, both of which are interconnected with the expression and function of other viral proteins. Emphasis is also given to the potential implication of these proteins in the maintenance of chronic infection in infected individuals. In light of recent findings, the discovery of these new genes opens a new avenue for the future treatment of HTLV-1- and HIV-1-infected individuals.

Sticky microbes: forces in microbial cell adhesion
Yves F. Dufrêne

Abstract

Understanding the fundamental forces involved in the adhesion of microbial cells is important not only in microbiology, to elucidate cellular functions (such as ligand-binding or biofilm formation), but also in medicine (biofilm infections) and biotechnology (cell aggregation). Rapid progress in atomic force microscopy (AFM) techniques has made it possible to measure the forces driving cell–cell and cell–substrate interactions on a single cell basis. A living cell is attached to the AFM probe, thereby enabling researchers to measure the interaction forces between the cell and a target surface. Recent advances in our understanding of the forces driving cell adhesion and biofilm formation are discussed, with a focus on pathogens. These studies provide compelling evidence that, upon contact with a surface, cell adhesion components display a variety of mechanical responses that are important for cell adhesion.
Getting to the root of epidemic spread with phylodynamic analysis of genomic data
Louis du Plessis, Tanja Stadler

Abstract

When epidemiological and evolutionary dynamics occur on similar timescales, pathogen genomes sampled from infected hosts carry a signature of the dynamics of epidemic spread. Phylodynamic inference methods aim to extract this signature from genetic data. We discuss the contribution of phylodynamics toward understanding the 2014 West African Ebola virus epidemic.

How Ebola has been evolving in West Africa
Si-Qing Liu, Simon Rayner, Bo Zhang

Abstract

The ongoing Ebola outbreak in West Africa has generated fears of a global epidemic. Particularly, estimates of higher substitution rates have raised concerns about increased transmissibility or virulence. A recent study using a more comprehensive datasets demonstrates lower variation, highlighting the importance of representative datasets and limitations of computational modelling.

Infectious asthma triggers: time to revise the hygiene hypothesis?
Wilmore C. Webley, Kelly L. Aldridge

Abstract

The hygiene hypothesis supports an inverse relationship between respiratory infections in early-life and atopic diseases. However, a recent study supports growing evidence that early-life infection and airway microbiome composition can significantly influence asthma inception and exacerbation later in life. This reignites discussions on infection-mediated asthma phenotypes and potential therapeutics.

Emerging intracellular receptors for hemorrhagic fever viruses
Lucas T. Jae, Thijn R. Brummelkamp

Abstract

Ebola virus and Lassa virus belong to different virus families that can cause viral hemorrhagic fever, a life-threatening disease in humans with limited treatment options. To infect a target cell, Ebola and Lassa viruses engage receptors at the cell surface and are subsequently shuttled into the endosomal compartment. Upon arrival in late endosomes/lysosomes, the viruses trigger membrane fusion to release their genome into the cytoplasm. Although contact sites at the cell surface were recognized for Ebola virus and Lassa virus, it was postulated that Ebola virus requires a critical receptor inside the cell. Recent screens for host factors identified such internal receptors for both viruses: Niemann–Pick disease type C1 protein (NPC1) for Ebola virus and lysosome-associated membrane protein 1 (LAMP1) for Lassa virus. A cellular trigger is needed to permit binding of the viral envelope protein to these intracellular receptors. This ‘receptor switch’ represents a previously unnoticed step in virus entry with implications for host–pathogen interactions and viral tropism.
Collateral sensitivity of antibiotic-resistant microbes
Csaba Pal, Balazs Papp, Viktoria Lazar

Abstract

Understanding how evolution of microbial resistance towards a given antibiotic influences susceptibility to other drugs is a challenge of profound importance. By combining laboratory evolution, genome sequencing, and functional analyses, recent works have charted the map of evolutionary trade-offs between antibiotics and have explored the underlying molecular mechanisms. Strikingly, mutations that caused multidrug resistance in bacteria simultaneously enhanced sensitivity to many other unrelated drugs (collateral sensitivity). Here, we explore how this emerging research sheds new light on resistance mechanisms and the way it could be exploited for the development of alternative antimicrobial strategies.

The changing face of asthma and its relation with microbes
Chris S. Earl, Shi-qi An, Robert P. Ryan

Abstract

During the past 50 years, the prevalence of asthma has increased and this has coincided with our changing relation with microorganisms. Asthma is a complex disease associated with local tissue inflammation of the airway that is determined by environmental, immunological, and host genetic factors. In a subgroup of sufferers, respiratory infections are associated with the development of chronic disease and more frequent inflammatory exacerbations. Recent studies suggest that these infections are polymicrobial in nature. Furthermore, there is increasing evidence that the recently discovered asthma airway microbiota may play a critical role in pathophysiological processes associated with the disease. Here, we discuss the current data regarding a possible role for infection in chronic asthma with a particular focus on the role bacteria may play. We discuss recent advances that are beginning to elucidate the complex relations between the microbiota and the immune response in asthma patients. We also highlight the clinical implications of these recent findings in regards to the development of novel therapeutic strategies.

Resistance is not futile: gliotoxin biosynthesis, functionality and utility
Stephen K. Dolan, Grainne O’Keeffe, Gary W. Jones, Sean Doyle

Abstract

Gliotoxin biosynthesis is encoded by the gli gene cluster in Aspergillus fumigatus. The biosynthesis of gliotoxin is influenced by a suite of transcriptionally-active regulatory proteins and a bis-thiomethyltransferase. A self-protection system against gliotoxin is present in A. fumigatus. Several additional metabolites are also produced via the gliotoxin biosynthetic pathway. Moreover, the biosynthesis of unrelated natural products appears to be influenced either by gliotoxin or by the activity of specific reactions within the biosynthetic pathway. The activity of gliotoxin against animal cells and fungi, often mediated by interference with redox homeostasis or protein modification, is revealing new metabolic interactions within eukaryotic systems. Nature has provided a most useful natural product with which to reveal some of its many molecular secrets.

Improving preclinical models of HIV microbicide efficacy
Nadia R. Roan, Jan Münch

Abstract

Despite potent in vitro efficacy, most topical microbicides fail to effectively prevent HIV transmission. One reason for clinical failure may be that current microbicide testing does not reflect the environment encountered during sexual virus transmission. We discuss how preclinical microbicide development could be improved by more closely mimicking real-life conditions.
Multipurpose prevention technologies: the future of HIV and STI protection
José A. Fernández-Romero, Carolyn Deal, Betsy C. Herold, John Schiller, Dorothy Patton, Thomas Zydowsky, Joe Romano, Christopher D. Petro, Manjulaa Narasimhan

Abstract
Every day, more than 1 million people are newly infected with sexually transmitted infections (STIs) that can lead to morbidity, mortality, and an increased risk of human immunodeficiency virus (HIV) acquisition. Existing prevention and management strategies, including behavior change, condom promotion, and therapy have not reduced the global incidence and prevalence, pointing to the need for novel innovative strategies. This review summarizes important issues raised during a satellite session at the first HIV Research for Prevention (R4P) conference, held in Cape Town, on October 31, 2014. We explore key STIs that are challenging public health today, new biomedical prevention approaches including multipurpose prevention technologies (MPTs), and the scientific and regulatory hurdles that must be overcome to make combination prevention tools a reality.

Staphylococcus aureus infections: transmission within households and the community
Justin Knox, Anne-Catrin Uhlemann, Franklin D. Lowy

Abstract
Staphylococcus aureus, both methicillin susceptible and resistant, are now major community-based pathogens worldwide. The basis for this is multifactorial and includes the emergence of epidemic clones with enhanced virulence, antibiotic resistance, colonization potential, or transmissibility. Household reservoirs of these unique strains are crucial to their success as community-based pathogens. Staphylococci become resident in households, either as colonizers or environmental contaminants, increasing the risk for recurrent infections. Interactions of household members with others in different households or at community sites, including schools and daycare facilities, have a critical role in the ability of these strains to become endemic. Colonization density at these sites appears to have an important role in facilitating transmission. The integration of research tools, including whole-genome sequencing (WGS), mathematical modeling, and social network analysis, has provided additional insight into the transmission dynamics of these strains. Thus far, interventions designed to reduce recurrent infections among household members have had limited success, likely due to the multiplicity of potential sources for recolonization. The development of better strategies to reduce the number of household-based infections will depend on greater insight into the different factors that contribute to the success of these uniquely successful epidemic clones of S. aureus.

Volume 23, Issue 8, August 2015

Lokiarchaeota: eukaryote-like missing links from microbial dark matter?
Arshan Nasir, Kyung Mo Kim, Gustavo Caetano-Anollés

Abstract
Identification and genome sequencing of novel organismal groups can reduce the gap between the sequenced minority and the unexplored majority. The recent discovery of phylum Lokiarchaeota promises understanding of biological history. Here we inquire if Lokiarchaeota truly represent ancient eukaryotic ancestors or just microbial dark matter of expanding archaeal diversity.
The giant panda gut microbiome
Fuwen Wei, Xiao Wang, Qi Wu

Abstract

Giant pandas (*Ailuropoda melanoleuca*) are bamboo specialists that evolved from carnivores. Their gut microbiota probably aids in the digestion of cellulose and this is considered an example of gut microbiota adaptation to a bamboo diet. However, this issue remains unresolved and further functional and compositional studies are needed.

Entry and exit of bacterial outer membrane proteins
Rajeev Misra

Abstract

The sites of new outer membrane protein (OMP) deposition and the fate of pre-existing OMPs are still enigmatic despite numerous concerted efforts. Rassam *et al.* identified mid-cell regions as the primary entry points for new OMP insertion in clusters, driving the pre-existing OMP clusters towards cell poles for long-term storage.

Is *Campylobacter* to esophageal adenocarcinoma as *Helicobacter* is to gastric adenocarcinoma?
Nadeem O. Kaakoush, Natalia Castaño-Rodríguez, Si Ming Man, Hazel M. Mitchell

Abstract

Esophageal adenocarcinoma develops through a cascade of cellular changes that shares similarities to the etiology of *Helicobacter pylori*-associated intestinal-type gastric adenocarcinoma. While host genetics and immune response have been implicated in the progression to esophageal adenocarcinoma, studies investigating esophageal microbial communities suggest that bacteria may also play an important role in driving the inflammation that leads to disease. Of these, emerging *Campylobacter* species have been found to be more prevalent and abundant in patients progressing through the esophageal adenocarcinoma cascade compared to controls. Given that these bacteria possess several virulence mechanisms such as toxin production, cellular invasion, and intracellular survival, emerging *Campylobacter* species should be investigated as etiological agents of the chronic esophageal inflammation that leads to cancer.

Evolution of bacterial transcription factors: how proteins take on new tasks, but do not always stop doing the old ones
Sandhya S. Visweswariah, Stephen J.W. Busby

Abstract

Many bacterial transcription factors do not behave as per the textbook operon model. We draw on whole genome work, as well as reported diversity across different bacteria, to argue that transcription factors may have evolved from nucleoid-associated proteins. This view would explain a large amount of recent data gleaned from high-throughput sequencing and bioinformatic analyses.
Bat-to-human: spike features determining ‘host jump’ of coronaviruses SARS-CoV, MERS-CoV, and beyond
Guangwen Lu, Qihui Wang, George F. Gao
Abstract

Both severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) are zoonotic pathogens that crossed the species barriers to infect humans. The mechanism of viral interspecies transmission is an important scientific question to be addressed. These coronaviruses contain a surface-located spike (S) protein that initiates infection by mediating receptor-recognition and membrane fusion and is therefore a key factor in host specificity. In addition, the S protein needs to be cleaved by host proteases before executing fusion, making these proteases a second determinant of coronavirus interspecies infection. Here, we summarize the progress made in the past decade in understanding the cross-species transmission of SARS-CoV and MERS-CoV by focusing on the features of the S protein, its receptor-binding characteristics, and the cleavage process involved in priming.

Whole-genome sequence comparisons reveal the evolution of Vibrio cholerae O1
Eun Jin Kim, Chan Hee Lee, G. Balakrish Nair, Dong Wook Kim
Abstract

The analysis of the whole-genome sequences of Vibrio cholerae strains from previous and current cholera pandemics has demonstrated that genomic changes and alterations in phage CTX (particularly in the gene encoding the B subunit of cholera toxin) were major features in the evolution of V. cholerae. Recent studies have revealed the genetic mechanisms in these bacteria by which new variants of V. cholerae are generated from type-specific strains; these mechanisms suggest that certain strains are selected by environmental or human factors over time. By understanding the mechanisms and driving forces of historical and current changes in the V. cholerae population, it would be possible to predict the direction of such changes and the evolution of new variants; this has implications for the battle against cholera.

Nitrogen cycling in corals: the key to understanding holobiont functioning?
Nils Rädecker, Claudia Pogoreutz, Christian R. Voolstra, Jörg Wiedenmann, Christian Wild
Abstract

Corals are animals that form close mutualistic associations with endosymbiotic photosynthetic algae of the genus Symbiodinium. Together they provide the calcium carbonate framework of coral reef ecosystems. The importance of the microbiome (i.e., bacteria, archaea, fungi, and viruses) to holobiont functioning has only recently been recognized. Given that growth and density of Symbiodinium within the coral host is highly dependent on nitrogen availability, nitrogen-cycling microbes may be of fundamental importance to the stability of the coral–algae symbiosis and holobiont functioning, in particular under nutrient-enriched and -depleted scenarios. We summarize what is known about nitrogen cycling in corals and conclude that disturbance of microbial nitrogen cycling may be tightly linked to coral bleaching and disease.

Tackling antimicrobial resistance at global and local scales
Hellen Gelband, Ramanan Laxminarayan
Abstract

Antibiotic resistance, similar to climate change, is a shared global problem, but unlike climate change, national and local action produces direct localized benefits in addition to improving the global situation.
Tolerance engineering in bacteria for the production of advanced biofuels and chemicals
Aindrila Mukhopadhyay

Abstract

During microbial production of solvent-like compounds, such as advanced biofuels and bulk chemicals, accumulation of the final product can negatively impact the cultivation of the host microbe and limit the production levels. Consequently, improving solvent tolerance is becoming an essential aspect of engineering microbial production strains. Mechanisms ranging from chaperones to transcriptional factors have been used to obtain solvent-tolerant strains. However, alleviating growth inhibition does not invariably result in increased production. Transporters specifically have emerged as a powerful category of proteins that bestow tolerance and often improve production but are difficult targets for cellular expression. Here we review strain engineering, primarily as it pertains to bacterial solvent tolerance, and the benefits and challenges associated with the expression of membrane-localized transporters in improving solvent tolerance and production.

RNA structures are involved in the thermoregulation of bacterial virulence-associated traits
María Victoria Grosso-Becera, Luis Servín-González, Gloria Soberón-Chávez

Abstract

Pathogenic bacteria are exposed to temperature changes during colonization of the human body and during exposure to environmental conditions. Virulence-associated traits are mainly expressed by pathogenic bacteria at 37°C. We review different cases of post-transcriptional regulation of virulence-associated proteins through RNA structures (called RNA thermometers or RNATs) that modulate the translation of mRNAs. The analysis of RNATs in pathogenic bacteria has started to produce a comprehensive picture of the structures involved, and of the genes regulated by this mechanism. However, we are still not able to predict the functionality of putative RNATs predicted by bioinformatics methods, and there is not a global approach to measure the effect of these RNA structures in gene regulation during bacterial infections.

Volume 23, Issue 9, September 2015

Languages and dialects: bacterial communication beyond homoserine lactones
Sophie Brameyer, Helge B. Bode, Ralf Heermann

Abstract

Gram-negative bacteria use N-acyl homoserine lactones (acyl-HSLs) for communication, predominantly mediated by LuxR-type receptors. Recent studies uncovered aryl-HSLs, α-pyrones and dialkylresorcinols as further chemical languages of Gram-negative bacteria. These findings extend the number of bacterial signaling molecules and suggest that cell–cell communication goes far beyond acyl-HSL signaling in nature.

Targeting specific bacteria in the oral microbiome
Jorge Frias-Lopez

Abstract

A lack of tools that kill selected members of the oral microbiome has hampered the ability to study specific roles of bacteria within bacterial communities. Work by Guo et al. shows the potential of antimicrobial peptides as a tool to assess the role of individual species in the microbial community.
Complex host genetic susceptibility to Staphylococcus aureus infections
Sanjay K. Shukla, Warren Rose, Steven J. Schrodi

Abstract

Understanding of the host genetic susceptibility to carriage of, and infections, due to Staphylococcus aureus, a nosocomial pathogen, is still in its nascent stages. Mouse models show variable susceptibility to S. aureus infections across mouse strains and disease models with roles for signaling pathways involving Toll-like receptors (TLR-1, TLR-2, and TLR-6), interleukins (IL-4, IL-6, IL-10, and IL-13), chemokines [CXC ligand (CXCL)-1 and CXCL-2], and T helper (Th)1/Th2 responses. Genome-wide association studies (GWASs) for carriage in humans identified SNPs in IL4, DEFB1, CRP, and VDR for persistent nasal carriage. NR3C1 haplotypes may either enhance risk or provide protection from colonization. GWASs for all S. aureus diseases have suggested roles for DAPK3, a kinase, and XRN1, a nuclease, while CDON could have a role in complicated bacteremia. More studies are needed to identify host susceptibility genes along with confirmation from functional assays.

The potential impact of coinfection on antimicrobial chemotherapy and drug resistance
Ruthie B. Birger, Roger D. Kouyos, Ted Cohen, Emily C. Griffiths, Silvie Huijben, Michael J. Mina, Victoriya Volkova, Bryan Grenfell, C. Jessica E. Metcalf

Abstract

Across a range of pathogens, resistance to chemotherapy is a growing problem in both public health and animal health. Despite the ubiquity of coinfection, and its potential effects on within-host biology, the role played by coinfecting pathogens on the evolution of resistance and efficacy of antimicrobial chemotherapy is rarely considered. In this review, we provide an overview of the mechanisms of interaction of coinfecting pathogens, ranging from immune modulation and resource modulation, to drug interactions. We discuss their potential implications for the evolution of resistance, providing evidence in the rare cases where it is available. Overall, our review indicates that the impact of coinfection has the potential to be considerable, suggesting that this should be taken into account when designing antimicrobial drug treatments.

Bacterial cellulose biosynthesis: diversity of operons, subunits, products, and functions
Ute Römling, Michael Y. Galperin

Abstract

Recent studies of bacterial cellulose biosynthesis, including structural characterization of a functional cellulose synthase complex, provided the first mechanistic insight into this fascinating process. In most studied bacteria, just two subunits, BcsA and BcsB, are necessary and sufficient for the formation of the polysaccharide chain in vitro. Other subunits – which differ among various taxa – affect the enzymatic activity and product yield in vivo by modulating (i) the expression of the biosynthesis apparatus, (ii) the export of the nascent β-D-glucan polymer to the cell surface, and (iii) the organization of cellulose fibers into a higher-order structure. These auxiliary subunits play key roles in determining the quantity and structure of resulting biofilms, which is particularly important for the interactions of bacteria with higher organisms – leading to rhizosphere colonization and modulating the virulence of cellulose-producing bacterial pathogens inside and outside of host cells. We review the organization of four principal types of cellulose synthase operon found in various bacterial genomes, identify additional bcs genes that encode components of the cellulose biosynthesis and secretion machinery, and propose a unified nomenclature for these genes and subunits. We also discuss the role of cellulose as a key component of biofilms and in the choice between acute infection and persistence in the host.
**Bacterial spread from cell to cell: beyond actin-based motility**
Carole J. Kuehl, Ana-Maria Dragoi, Arthur Talman, Hervé Agaisse

Abstract

Several intracellular pathogens display the ability to propagate within host tissues by displaying actin-based motility in the cytosol of infected cells. As motile bacteria reach cell–cell contacts they form plasma membrane protrusions that project into adjacent cells and resolve into vacuoles from which the pathogen escapes, thereby achieving spread from cell to cell. Seminal studies have defined the bacterial and cellular factors that support actin-based motility. By contrast, the mechanisms supporting the formation of protrusions and their resolution into vacuoles have remained elusive. Here, we review recent advances in the field showing that *Listeria monocytogenes* and *Shigella flexneri* have evolved pathogen-specific mechanisms of bacterial spread from cell to cell.

**Control of bacterial metabolism by quorum sensing**
Eunhye Goo, Jae Hyung An, Yongsung Kang, Ingyu Hwang

Abstract

Bacterial quorum sensing (QS)-dependent gene expression is a dynamic response to cell density. Bacteria produce costly public goods for the benefit of the population as a whole. As an example, QS rewires cellular metabolism to produce oxalate (a public good) to enable survival during the stationary phase in *Burkholderia glumae*, *Burkholderia thailandensis*, and *Burkholderia pseudomallei*. Recent reports showed that QS serves as a metabolic brake to maintain homeostatic primary metabolism in *B. glumae* and readjusts the central metabolism of *Pseudomonas aeruginosa*. In this review, we emphasize the dynamics and complexity of the control of gene expression by QS and discuss the metabolic costs and possible metabolic options to sustain cooperativity. We then focus on how QS influences bacterial central metabolism.

**How do divergent ecological strategies emerge among marine bacterioplankton lineages?**
Haiwei Luo, Mary Ann Moran

Abstract

Heterotrophic bacteria in pelagic marine environments are frequently categorized into two canonical ecological groups: patch-associated and free-living. This framework provides a conceptual basis for understanding bacterial utilization of oceanic organic matter. Some patch-associated bacteria are ecologically linked with eukaryotic phytoplankton, and this observation fits with predicted coincidence of their genome expansion with marine phytoplankton diversification. By contrast, free-living bacteria in today's oceans typically live singly with streamlined metabolic and regulatory functions that allow them to grow in nutrient-poor seawater. Recent analyses of marine Alphaproteobacteria suggest that some free-living bacterioplankton lineages evolved from patch-associated ancestors up to several hundred million years ago. While evolutionary analyses agree with the hypothesis that natural selection has maintained these distinct ecological strategies and genomic traits in present-day populations, they do not rule out a major role for genetic drift in driving ancient ecological switches. These two evolutionary forces may have acted on ocean bacteria at different geological time scales and under different geochemical constraints, with possible implications for future adaptations to a changing ocean. New evolutionary models and genomic data are leading to a more comprehensive understanding of marine bacterioplankton evolutionary history.
The Tailocin Tale: Peeling off Phage Tails
Maarten G.K. Ghequire, René De Mot

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Bacteria produce a variety of particles resembling phage tails that are functional without an associated phage head. Acquired from diverse bacteriophage sources, these stand-alone units were sculpted to serve different ecological roles. Such tailocins mediate antagonism between related bacteria as well as interactions with eukaryotic cells.

SRFBP1, an Additional Player in HCV Entry
Lucie Fénéant, Laurence Cocquerel

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The tetraspanin CD81 dynamics and interactions with other proteins are essential for hepatitis C virus (HCV) entry. Recently, Gerold and collaborators used a proteomic approach and found the serum response factor binding protein 1 (SRFBP1) to be involved in a post-fusion entry process by interacting with CD81 upon HCV infection.

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Valerie Le Sage, Alessandro Cinti, Andrew J. Mouland

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Production of infectious HIV-1 particles requires viral envelope (Env) glycoprotein incorporation. Although, the precise mechanism remains elusive, interaction between Env and the matrix (MA) domain of Gag plays a central role. Work by Mu and colleagues demonstrates how the Env–MA interaction regulates gag mRNA stability and Gag expression levels.

Rerouting Resistance: Escaping Restriction Using Alternative Cellular Pathways
Ailie Marx, Akram Alian

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Pathogens, essentially utilizing host machinery for replication, can adapt to exploit cellular redundancies to substitute favored host–pathogen interactions when blocked, leading to a new type of stubborn resistance. Resa-Infante et al. reveal one such ‘rerouting-resistance’ acquired by the influenza virus when a vital host factor was deleted in mice.

Rates of Lateral Gene Transfer in Prokaryotes: High but Why?
Michiel Vos, Matthijn C. Hesselman, Tim A. te Beek, Mark W.J. van Passel, Adam Eyre-Walker

Abstract
Lateral gene transfer is of fundamental importance to the evolution of prokaryote genomes and has important practical consequences, as evidenced by the rapid dissemination of antibiotic resistance and virulence determinants. Relatively little effort has so far been devoted to explicitly quantifying the rate at which accessory genes are taken up and lost, but it is possible that the combined rate of lateral gene transfer and gene loss is higher than that of point mutation. What evolutionary forces underlie the rate of lateral gene transfer are not well understood. We here use theory developed to explain the evolution of mutation rates to address this question and explore its consequences for the study of prokaryote evolution.
Engineering Microbiomes to Improve Plant and Animal Health
U.G. Mueller, J.L. Sachs

Abstract

Animal and plant microbiomes encompass diverse microbial communities that colonize every accessible host tissue. These microbiomes enhance host functions, contributing to host health and fitness. A novel approach to improve animal and plant fitness is to artificially select upon microbiomes, thus engineering evolved microbiomes with specific effects on host fitness. We call this engineering approach host-mediated microbiome selection, because this method selects upon microbial communities indirectly through the host and leverages host traits that evolved to influence microbiomes. In essence, host phenotypes are used as probes to gauge and manipulate those microbiome functions that impact host fitness. To facilitate research on host-mediated microbiome engineering, we explain and compare the principal methods to impose artificial selection on microbiomes; discuss advantages and potential challenges of each method; offer a skeptical appraisal of each method in light of these potential challenges; and outline experimental strategies to optimize microbiome engineering. Finally, we develop a predictive framework for microbiome engineering that organizes research around principles of artificial selection, quantitative genetics, and microbial community-ecology.

Roles of Lipoproteins and Apolipoproteins in Particle Formation of Hepatitis C Virus
Takasuke Fukuhara, Chikako Ono, Francesc Puig-Basagoiti, Yoshiharu Matsuura

Abstract

More than 160 million people worldwide are infected with hepatitis C virus (HCV), and cirrhosis and hepatocellular carcinoma induced by HCV infection are life-threatening diseases. HCV takes advantage of many aspects of lipid metabolism for an efficient propagation in hepatocytes. Due to the morphological and physiological similarities of HCV particles to lipoproteins, lipid-associated HCV particles are named lipoviroparticles. Recent analyses have revealed that exchangeable apolipoproteins directly interact with the viral membrane to generate infectious HCV particles. In this review, we summarize the roles of lipid metabolism in the life cycle of HCV.

Sweet Talk: Protein Glycosylation in Bacterial Interaction With the Host
Qiuhe Lu, Shan Li, Feng Shao

Abstract

Pathogenic bacteria encode virulent glycosyltransferases that conjugate various glycans onto substrate proteins via the N- or O-linkage. The HMW system in nontypeable Haemophilus influenzae and the Pgl system in Campylobacter jejuni glycosylate bacterial surface or periplasmic proteins at the eukaryotic-like Asn-X-Ser/Thr motif. The NleB effector from enterobacteria mediates arginine GlcNAcylation of host death-domain proteins to block inflammation, representing an atypical N-glycosylation. The large clostridial cytotoxins and related glucosyltransferase toxins from Legionella and Photorhabdus monoglycosylate a serine/threonine or tyrosine in host Rho GTPase or elongation factor 1A (eEF1A). The emerging bacterial autotransporter heptosyltransferase (BAHT) family of heptosyltransferases also catalyses O-glycosylation and modifies autotransporters for adhesion to the host. These glycosylations, diverse in linkages and glycan structures, determine appropriate functioning of bacterial virulence factors or hijack host cellular processes in pathogenesis.
Natural Product Biosynthetic Diversity and Comparative Genomics of the Cyanobacteria
Elke Dittmann, Muriel Gugger, Kaarina Sivonen, David P. Fewer

Abstract

Cyanobacteria are an ancient lineage of slow-growing photosynthetic bacteria and a prolific source of natural products with intricate chemical structures and potent biological activities. The bulk of these natural products are known from just a handful of genera. Recent efforts have elucidated the mechanisms underpinning the biosynthesis of a diverse array of natural products from cyanobacteria. Many of the biosynthetic mechanisms are unique to cyanobacteria or rarely described from other organisms. Advances in genome sequence technology have precipitated a deluge of genome sequences for cyanobacteria. This makes it possible to link known natural products to biosynthetic gene clusters but also accelerates the discovery of new natural products through genome mining. These studies demonstrate that cyanobacteria encode a huge variety of cryptic gene clusters for the production of natural products, and the known chemical diversity is likely to be just a fraction of the true biosynthetic capabilities of this fascinating and ancient group of organisms.

Antiviral Monoclonal Antibodies: Can They Be More Than Simple Neutralizing Agents?
Mireia Pelegrin, Mar Naranjo-Gomez, Marc Piechaczyk

Abstract

Monoclonal antibodies (mAbs) are increasingly being considered as agents to fight severe viral diseases. So far, they have essentially been selected and used on the basis of their virus-neutralizing activity and/or cell-killing activity to blunt viral propagation via direct mechanisms. There is, however, accumulating evidence that they can also induce long-lasting protective antiviral immunity by recruiting the endogenous immune system of infected individuals during the period of immunotherapy. Exploiting this property may revolutionize antiviral mAb-based immunotherapies, with benefits for both patients and healthcare systems.

Volume 23, Issue 10, October 2015

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Volume 23, Issue 11, November 2015

Biofilm Recruitment of Vibrio cholerae by Matrix Proteolysis
Marylise Duperthuy, Bernt Eric Uhlin, Sun Nyunt Wai

Abstract

The appearance of bacterial biofilms involves secretion of polysaccharides and proteins that form an extracellular matrix embedding the bacteria. Proteases have also been observed, but their role has remained unclear. Smith and co-workers have now found that proteolysis can contribute to further recruitment of bacteria to Vibrio cholerae biofilms.

One of These is Not Like the Others
Martin S. Pavelka Jr

Abstract

A Mycobacterium tuberculosis metA mutant that is auxotrophic for methionine is unlike other auxotrophic mutants of this important species as methionine starvation results in rapid death instead of cessation of growth. Evidence suggests that this phenotype results from starvation affecting essential pathways that utilize S-adenosylmethionine in addition to methionine.

Microbial Malaise: How Can We Classify the Microbiome?
Robert G. Beiko

Abstract

The names and lineages of microorganisms are critical to our understanding of the microbiome. However, microbial taxonomy and phylogeny are in perpetual flux, with emerging criteria being used to rename and reshape our views of the microbial world. Different candidate molecular and nonmolecular criteria are often broadly consistent with one another, which underpins the pluralistic approach to taxonomy. However, the taxonomic picture is clouded when underlying criteria are not in agreement, or when reference datasets contain erroneously named organisms. How does the shifting taxonomic landscape impact our interpretation of microbial communities, especially in the face of inconsistencies and errors? How can taxonomy be applied in a consistent way when different users have different requirements of the classifications that emerge? The key path forward involves finding ways to integrate conflicting taxonomic criteria, choosing the right units of analysis for microbiomic studies, and making molecular taxonomy transparent and accessible in a way that complements current genomic resources.
**SAMHD1: At the Crossroads of Cell Proliferation, Immune Responses, and Virus Restriction**

Ester Ballana, José A. Esté

**Abstract**

SAMHD1 is a triphosphohydrolase enzyme that controls the intracellular level of deoxyribonucleoside triphosphates (dNTPs) and plays a role in innate immune sensing and autoimmune disease. SAMHD1 has also been identified as an intrinsic virus restriction factor, inactivated through degradation by HIV-2 Vpx or through a post-transcriptional regulatory mechanism. Phosphorylation of SAMHD1 by cyclin-dependent kinases has been strongly associated with inactivation of the virus restriction mechanism, providing an association between virus replication and cell proliferation. Tight regulation of cell proliferation suggests that viruses, particularly HIV-1 replication, latency, and reactivation, may be similarly controlled by multiple checkpoint mechanisms that, in turn, regulate dNTP levels. In this review, we discuss how SAMHD1 is a viral restriction factor, the mechanism associated with viral restriction, the pathway leading to its inactivation in proliferating cells, and how strategies aimed at controlling virus restriction could lead to a functional cure for HIV.

**Bacterial Amyloid Formation: Structural Insights into Curli Biogenesis**

Nani Van Gerven, Roger D. Klein, Scott J. Hultgren, Han Remaut

**Abstract**

Curli are functional amyloid fibers assembled by many Gram-negative bacteria as part of an extracellular matrix that encapsulates the bacteria within a biofilm. A multicomponent secretion system ensures the safe transport of the aggregation-prone curli subunits across the periplasm and outer membrane, and coordinates subunit self-assembly into surface-attached fibers. To avoid the build-up of potentially toxic intracellular protein aggregates, the timing and location of the interactions of the different curli proteins are of paramount importance. Here we review the structural and molecular biology of curli biogenesis, with a focus on the recent breakthroughs in our understanding of subunit chaperoning and secretion. The mechanistic insight into the curli assembly pathway will provide tools for new biotechnological applications and inform the design of targeted inhibitors of amyloid polymerization and biofilm formation.

**Roles of Indole as an Interspecies and Interkingdom Signaling Molecule**

Jin-Hyung Lee, Thomas K. Wood, Jintae Lee

**Abstract**

A number of bacteria, and some plants, produce large quantities of indole, which is widespread in animal intestinal tracts and in the rhizosphere. Indole, as an interspecies and interkingdom signaling molecule, plays important roles in bacterial pathogenesis and eukaryotic immunity. Furthermore, indole and its derivatives are viewed as potential antivirulence compounds against antibiotic-resistant pathogens because of their ability to inhibit quorum sensing and virulence factor production. Indole modulates oxidative stress, intestinal inflammation, and hormone secretion in animals, and it controls plant defense systems and growth. Insects and nematodes can recognize indole, which controls some of their behavior. This review presents current knowledge regarding indole and its derivatives, their biotechnological applications and their role in prokaryotic and eukaryotic systems.

**Microbial Invasions: The Process, Patterns, and Mechanisms**

Cyrus Alexander Mallon, Jan Dirk van Elsas, Joana Falcão Salles

**Abstract**

There has recently been a surge of literature examining microbial invasions into a variety of environments. These studies often include a component of biological diversity as a major factor determining an invader's fate, yet common results are rarely cross-compared. Since many studies only present a snapshot of the entire invasion process, a bird's eye view is required to piece together the entire continuum, which we find consists of introduction, establishment, spread, and impact phases. We further examine the patterns and mechanisms associated with invasion resistance and create a mechanistic synthesis governed by the species richness, species evenness, and resource availability of resident communities. We conclude by exploring the advantages of using a theoretical invasion framework across different fields.
Ten Years of Maintaining and Expanding a Microbial Genome and Metagenome Analysis System
Victor M. Markowitz, I-Min A. Chen, Ken Chu, Amrita Pati, Natalia N. Ivanova, Nikos C. Kyrpides

Abstract

Launched in March 2005, the Integrated Microbial Genomes (IMG) system is a comprehensive data management system that supports multidimensional comparative analysis of genomic data. At the core of the IMG system is a data warehouse that contains genome and metagenome datasets sequenced at the Joint Genome Institute or provided by scientific users, as well as public genome datasets available at the National Center for Biotechnology Information Genbank sequence data archive. Genomes and metagenome datasets are processed using IMG's microbial genome and metagenome sequence data processing pipelines and are integrated into the data warehouse using IMG's data integration toolkits. Microbial genome and metagenome application specific data marts and user interfaces provide access to different subsets of IMG's data and analysis toolkits. This review article revisits IMG's original aims, highlights key milestones reached by the system during the past 10 years, and discusses the main challenges faced by a rapidly expanding system, in particular the complexity of maintaining such a system in an academic setting with limited budgets and computing and data management infrastructure.

Volume 23, Issue 12, December 2015

Programming Bacteriophages by Swapping Their Specificity Determinants
Moran G. Goren, Ido Yosef, Udi Qimron

Abstract

Bacteriophages, bacteria's natural enemies, may serve as potent antibacterial agents. Their specificity for certain bacterial sub-species limits their effectiveness, but allows selective targeting of bacteria. Lu and colleagues present a platform for such targeting through alteration of bacteriophages’ host specificity by swapping specificity domains in their host-recognition ligand.

Small Molecules Take A Big Step Against Clostridium difficile
Greg L. Beilhartz, John Tam, Roman A. Melnyk

Abstract

Effective treatment of Clostridium difficile infections demands a shift away from antibiotics towards toxin-neutralizing agents. Work by Bender et al., using a drug that attenuates toxin action in vivo without affecting bacterial survival, demonstrates the exciting potential of small molecules as a new modality in the fight against C. difficile.

Adipose Tissue: Sanctuary for HIV/SIV Persistence and Replication
Suresh Pallikkuth, Mahesh Mohan

Abstract

This commentary highlights new findings from a recent study identifying adipose tissue as a potential HIV reservoir and a major site of inflammation during chronic human/simian immunodeficiency virus (HIV/SIV) infection. A concise discussion about upcoming challenges and new research avenues for reducing chronic adipose inflammation during HIV/SIV infection is presented.
The Mineralosphere Concept: Mineralogical Control of the Distribution and Function of Mineral-associated Bacterial Communities
Stephane Uroz, Laura Catherine Kelly, Marie-Pierre Turpault, Cendrella Lepleux, Pascale Frey-Klett
Abstract

Soil is composed of a mosaic of different rocks and minerals, usually considered as an inert substrata for microbial colonization. However, recent findings suggest that minerals, in soils and elsewhere, favour the development of specific microbial communities according to their mineralogy, nutritive content, and weatherability. Based upon recent studies, we highlight how bacterial communities are distributed on the surface of, and in close proximity to, minerals. We also consider the potential role of the mineral-associated bacterial communities in mineral weathering and nutrient cycling in soils, with a specific focus on nutrient-poor and acidic forest ecosystems. We propose to define this microbial habitat as the mineralosphere, where key drivers of the microbial communities are the physicochemical properties of the minerals.

The HIV-1 Entry Process: A Stoichiometric View
Oliver F. Brandenberg, Carsten Magnus, Roland R. Regoes, Alexandra Trkola
Abstract

HIV-1 infection starts with fusion of the viral and the host cell membranes, a process mediated by the HIV-1 envelope glycoprotein trimer. The number of trimers required to complete membrane fusion, referred to as HIV-1 entry stoichiometry, remains under debate. A precise definition of HIV-1 entry stoichiometry is important as it reflects the efficacy of the viral entry process and steers the infectivity of HIV-1 virion populations. Initial estimates suggested a unanimous entry stoichiometry across HIV-1 strains while recent findings showed that HIV-1 strains can differ in entry stoichiometry. Here, we review current analyses of HIV-1 entry stoichiometry and point out future research directions to further define the interplay between entry stoichiometry, virus entry fitness, transmission, and susceptibility to antibody neutralization.

How Bacteria Use Type IV Pili Machinery on Surfaces
Berenike Maier, Gerard C.L. Wong
Abstract

The bacterial type IV pilus (T4P) is a versatile molecular machine with a broad range of functions. Recent advances revealed that the molecular components and the biophysical properties of the machine are well conserved among phylogenetically distant bacterial species. However, its functions are diverse, and include adhesion, motility, and horizontal gene transfer. This review focusses on the role of T4P in surface motility and bacterial interactions. Different species have evolved distinct mechanisms for intracellular coordination of multiple pili and of pili with other motility machines, ranging from physical coordination to biochemical clocks. Coordinated behavior between multiple bacteria on a surface is achieved by active manipulation of surfaces and modulation of pilus–pilus interactions. An emerging picture is that the T4P actively senses and responds to environmental conditions.

Stealing the Keys to the Kitchen: Viral Manipulation of the Host Cell Metabolic Network
Christopher M. Goodwin, Shihao Xu, Joshua Munger
Abstract

Host cells possess the metabolic assets required for viral infection. Recent studies indicate that control of the host's metabolic resources is a core host–pathogen interaction. Viruses have evolved mechanisms to usurp the host's metabolic resources, funneling them towards the production of virion components as well as the organization of specialized compartments for replication, maturation, and dissemination. Consequently, hosts have developed a variety of metabolic countermeasures to sense and resist these viral changes. The complex interplay between virus and host over metabolic control has only just begun to be deconvoluted. However, it is clear that virally induced metabolic reprogramming can substantially impact infectious outcomes, highlighting the promise of targeting these processes for antiviral therapeutic development.
Pentraxins and Collectins: Friend or Foe during Pathogen Invasion?
Suan-Sin Foo, Patrick C. Reading, Sébastien Jaillon, Alberto Mantovani, Suresh Mahalingam

Abstract

Innate immunity serves as the frontline defence against invading pathogens. Despite decades of research, new insights are constantly challenging our understanding of host-elicited immunity during microbial infections. Recently, two families of humoral innate immune proteins, pentraxins and collectins, have become a major focus of research in the field of innate immunity. Pentraxins and collectins are key players in activating the humoral arm of innate immunity, taking centre stage in immunoregulation and disease modulation. However, increasing evidence suggests that pentraxins and collectins can also mediate pathogenic effects during some infections. Herein, we discuss the protective and pathogenic effects of pentraxins and collectins, as well as their therapeutic significance.

Brucella abortus Cell Cycle and Infection Are Coordinated
Xavier De Bolle, Sean Crosson, Jean-Yves Matroule, Jean-Jacques Letesson

Abstract

Brucellae are facultative intracellular pathogens. The recent development of methods and genetically engineered strains allowed the description of cell-cycle progression of Brucella abortus, including unipolar growth and the ordered initiation of chromosomal replication. B. abortus cell-cycle progression is coordinated with intracellular trafficking in the endosomal compartments. Bacteria are first blocked at the G1 stage, growth and chromosome replication being resumed shortly before reaching the intracellular proliferation compartment. The control mechanisms of cell cycle are similar to those reported for the bacterium Caulobacter crescentus, and they are crucial for survival in the host cell. The development of single-cell analyses could also be applied to other bacterial pathogens to investigate their cell-cycle progression during infection.