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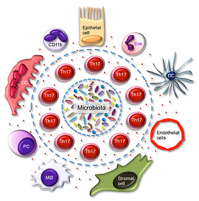
COVER IMAGE



Cover photograph: Functional interleukin-17 receptors (IL-17RS) are expressed on various cell types. Upon interaction with the host microbiota, T helper lymphocytes release IL-17, which affects healthy and neoplastic epithelial cells, eosinophils (Eos), dendritic cells (DC), endothelial cells, stromal cells, macrophages (MØ), healthy and neoplastic plasma cells (PC), osteoclasts (OC), and neutrophils or myeloid-derived suppressor cells (CD11b), eventually propelling immune-mediated inflammatory diseases (IMID) and cancer. Therefore, Th17 cells represent the missing link between host microbiota and IMIDs and cancer. (*See related article in June 2020, vol. 84, no. 2, e00064-19.*)

EDITORIAL

The ASM Journals Committee Values the Contributions of Black Microbiologists **e00122-20**
Patrick D. Schloss, Melissa Junior, Rebecca Alvania, Cesar A. Arias, Andreas Baumler, Arturo Casadevall, Corrella Detweiler, Harold Drake, Jack Gilbert, Michael J. Imperiale, Susan Lovett, Stanley Maloy, Alexander J. McAdam, Irene L. G. Newton, Michael J. Sadowsky, Rozanne M. Sandri-Goldin, Thomas J. Silhavy, Peter Tontonoz, Jo-Anne H. Young, Craig E. Cameron, Isaac Cann, A. Oveta Fuller, Ariangela J. Kozik

REVIEWS

A Comprehensive View of Translesion Synthesis in *Escherichia coli* **e00002-20**
Shingo Fujii, Robert P. Fuchs

Summary: The lesion bypass pathway, translesion synthesis (TLS), exists in essentially all organisms and is considered a pathway for postreplicative gap repair and, at the same time, for lesion tolerance. As with the saying "a trip is not over until you get back home," studying TLS only at the site of the lesion is not enough to understand the whole process of TLS. Recently, a genetic study uncovered that polymerase V (Pol V), a poorly expressed *Escherichia coli* TLS polymerase, is not only involved in the TLS step *per se* but also participates in the gap-filling reaction over several hundred nucleotides. The same study revealed that in contrast, Pol IV, another highly expressed TLS polymerase, essentially stays away from the gap-filling reaction. These observations imply fundamentally different ways these polymerases are recruited to DNA in cells. While access of Pol IV appears to be governed by mass action, efficient recruitment of Pol V involves a chaperone-like action of the RecA filament. We present a model of Pol V activation: the 3′ tip of the RecA filament initially stabilizes Pol V to allow stable complex formation with a sliding β-clamp, followed by the capture of the terminal RecA monomer by Pol V, thus forming a functional Pol V complex. This activation process likely determines higher accessibility of Pol V than of Pol IV to normal DNA. Finally, we discuss the biological significance of TLS polymerases during gap-filling reactions: error-prone gap-filling synthesis may contribute as a driving force for genetic diversity, adaptive mutation, and evolution.

RidA Proteins Protect against Metabolic Damage by Reactive Intermediates **e00024-20**
Jessica L. Irons, Kelsey Hodge-Hanson, Diana M. Downs

Summary: The Rid (YjgF/YER057c/UK114) protein superfamily was first defined by sequence homology with available protein sequences from bacteria, archaea, and eukaryotes (L. Parsons, N. Bonander, E. Eisenstein, M. Gilson, et al., Biochemistry 42: 80–89, 2003, https://doi.org/10.1021/bi020541w). The archetypal subfamily, RidA (reactive intermediate deaminase A), is found in all domains of life, with the vast majority of free-living organisms carrying at least one RidA homolog. In over 2

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decades, close to 100 reports have implicated Rid family members in cellular processes in prokaryotes, yeast, plants, and mammals. Functional roles have been proposed for Rid enzymes in amino acid biosynthesis, plant root development and nutrient acquisition, cellular respiration, and carcinogenesis. Despite the wealth of literature and over a dozen high-resolution structures of different RidA enzymes, their biochemical function remained elusive for decades. The function of the RidA protein was elucidated in a bacterial model system despite (i) a minimal phenotype of *ridA* mutants, (ii) the enzyme catalyzing a reaction believed to occur spontaneously, and (iii) confusing literature on the pleiotropic effects of RidA homologs in prokaryotes and eukaryotes. Subsequent work provided the physiological framework to support the RidA paradigm in *Salmonella enterica* by linking the phenotypes of mutants lacking *ridA* to the accumulation of the reactive metabolite 2-aminoacrylate (2AA), which damaged metabolic enzymes. Conservation of enamine/imine deaminase activity of RidA enzymes from all domains raises the likelihood that, despite the diverse phenotypes, the consequences when RidA is absent are due to accumulated 2AA (or a similar reactive enamine) and the diversity of metabolic phenotypes can be attributed to differences in metabolic network architecture. The discovery of the RidA paradigm in *S. enterica* laid a foundation for assessing the role of Rid enzymes in diverse organisms and contributed fundamental lessons on metabolic network evolution and diversity in microbes. This review describes the studies that defined the conserved function of RidA, the paradigm of enamine stress in *S. enterica*, and emerging studies that explore how this paradigm differs in other organisms. We focus primarily on the RidA subfamily, while remarking on our current understanding of the other Rid subfamilies. Finally, we describe the current status of the field and pose questions that will drive future studies on this widely conserved protein family to provide fundamental new metabolic information.

Staphylococcal Biofilm Development: Structure, Regulation, and Treatment Strategies **e00026-19**
Katrin Schilcher, Alexander R. Horswill

Summary: In many natural and clinical settings, bacteria are associated with some type of biotic or abiotic surface that enables them to form biofilms, a multicellular lifestyle with bacteria embedded in an extracellular matrix. *Staphylococcus aureus* and *Staphylococcus epidermidis*, the most frequent causes of biofilm-associated infections on indwelling medical devices, can switch between an existence as single free-floating cells and multicellular biofilms. During biofilm formation, cells first attach to a surface and then multiply to form microcolonies. They subsequently produce the extracellular matrix, a hallmark of biofilm formation, which consists of polysaccharides, proteins, and extracellular DNA. After biofilm maturation into three-dimensional structures, the biofilm community undergoes a disassembly process that leads to the dissemination of staphylococcal cells. As biofilms are dynamic and complex biological systems, staphylococci have evolved a vast network of regulatory mechanisms to modify and fine-tune biofilm development upon changes in environmental conditions. Thus, biofilm formation is used as a strategy for survival and persistence in the human host and can serve as a reservoir for spreading to new infection sites. Moreover, staphylococcal biofilms provide enhanced resilience toward antibiotics and the immune response and impose remarkable therapeutic challenges in clinics worldwide. This review provides an overview and an updated perspective on staphylococcal biofilms, describing the characteristic features of biofilm formation, the structural and functional properties of the biofilm matrix, and the most important mechanisms involved in the regulation of staphylococcal biofilm formation. Finally, we highlight promising strategies and technologies, including multitargeted or combinational therapies, to eradicate staphylococcal biofilms.

A Thermosensitive, Phase-Variable Epigenetic Switch: *pap* Revisited **e00030-17**
Mario Zamora, Christine A. Ziegler, Peter L. Freddolino, Alan J. Wolfe

Summary: It has been more than a decade since the last comprehensive review of the phase-variable uropathogen-associated pyelonephritis-associated pilus (*pap*) genetic switch. Since then, important data have come to light, including additional factors that regulate *pap* expression, better characterization of H-NS regulation, the structure of the Lrp octamer in complex with *pap* regulatory DNA, the temperature-insensitive phenotype of a mutant lacking the acetyltransferase RimJ, evidence that key components of the regulatory machinery are acetylated, and new insights into the role of DNA binding by key regulators in shaping both the physical structure and regulatory state of the *papI* and *papBA* promoters. This review revisits *pap*, integrating these newer observations with older ones to produce a new model for the concerted behavior of this virulence-regulatory region.