



CONTENTS • MARCH 2019 • VOLUME 63, NO. 3

CHEMISTRY; BIOSYNTHESIS

- Indole-2-Carboxamides Are Active against *Mycobacterium abscessus* in a Mouse Model of Acute Infection** e02245-18

Amit N. Pandya, Pavan K. Prathipati, Pooja Hegde, Wei Li, Kyle F. Graham, Subhra Mandal, Kristen M. Drescher, Christopher J. Destache, Diane Ordway, Mary Jackson, E. Jeffrey North

MECHANISMS OF ACTION: PHYSIOLOGICAL EFFECTS

- Isoniazid Bactericidal Activity Involves Electron Transport Chain Perturbation** e01841-18

Sheng Zeng, Karine Soetaert, Faustine Ravon, Marie Vandeput, Dirk Bald, Jean-Michel Kauffmann, Vanessa Mathys, Ruddy Wattiez, Véronique Fontaine

- Moxifloxacin in Chronic Obstructive Pulmonary Disease: Pharmacokinetics and Penetration into Bronchial Secretions in Ward and Intensive Care Unit Patients** e01974-18

Maria Sionidou, Katerina Manika, Georgia Pitsiou, Paschalina Kontou, Kalliopi Chatzika, Paul Zarogoulidis, Ioannis Kioumis

MECHANISMS OF RESISTANCE

- Vacuolar Sequestration of Azoles, a Novel Strategy of Azole Antifungal Resistance Conserved across Pathogenic and Nonpathogenic Yeast** e01347-18

Nitesh Kumar Khandelwal, Mohd Wasi, Remya Nair, Meghna Gupta, Mohit Kumar, Alok K. Mondal, Naseem A. Gaur, Rajendra Prasad

- Investigation of Novel *pmrB* and *eptA* Mutations in Isogenic *Acinetobacter baumannii* Isolates Associated with Colistin Resistance and Increased Virulence *In Vivo*** e01586-18

Stefanie Gerson, Jonathan W. Betts, Kai Lucaßen, Carolina Silva Nodari, Julia Wille, Michaele Josten, Stephan Göttig, Jennifer Nowak, Danuta Stefanik, Ignasi Roca, Jordi Vila, José M. Cisneros, Roberto M. La Ragione, Harald Seifert, Paul G. Higgins

- An IncR Plasmid Harbored by a Hypervirulent Carbapenem-Resistant *Klebsiella pneumoniae* Strain Possesses Five Tandem Repeats of the *bla*_{KPC-2}::NTE_{KPC-1d} Fragment** e01775-18

Ning Dong, Lizhang Liu, Rong Zhang, Kaichao Chen, Miaomiao Xie, Edward Wai Chi Chan, Sheng Chen

- Evolution of Daptomycin Resistance in Coagulase-Negative Staphylococci Involves Mutations of the Essential Two-Component Regulator WalkR** e01926-18

Jhih-Hang Jiang, Carina Dexter, David R. Cameron, Ian R. Monk, Sarah L. Baines, Iain J. Abbott, Denis W. Spelman, Xenia Kostoulas, Cara Nethercott, Benjamin P. Howden, Anton Y. Peleg

- Effects of KPC Variant and Porin Genotype on the *In Vitro* Activity of Meropenem-Vaborbactam against Carbapenem-Resistant *Enterobacteriaceae*** e02048-18

William R. Wilson, Ellen G. Kline, Chelsea E. Jones, Kristin T. Morder, Roberta T. Mettus, Yohei Doi, M. Hong Nguyen, Cornelius J. Clancy, Ryan K. Shields

- Clofazimine Exposure *In Vitro* Selects Efflux Pump Mutants and Bedaquiline Resistance** e02141-18

Nabila Ismail, Remco P. H. Peters, Nazir A. Ismail, Shaheed V. Omar

- Roles of Efflux Pumps from Different Superfamilies in the Surface-Associated Motility and Virulence of *Acinetobacter baumannii* ATCC 17978** e02190-18

María Pérez-Varela, Jordi Corral, Jesús Aranda, Jordi Barbé

- Emergence of OXA-232 Carbapenemase-Producing *Klebsiella pneumoniae* That Carries a pLVPK-Like Virulence Plasmid among Elderly Patients in China** e02246-18
Lingbin Shu, Ning Dong, Jun Lu, Zhiwei Zheng, Jie Hu, Wenqing Zeng, Qiaoling Sun, Edward Wai-Chi Chan, Hongwei Zhou, Fupin Hu, Sheng Chen, Rong Zhang
- Emergence of a Multidrug-Resistant Hypervirulent *Klebsiella pneumoniae* Sequence Type 23 Strain with a Rare *bla*_{CTX-M-24}-Harboring Virulence Plasmid** e02273-18
Dingxia Shen, Guannan Ma, Cuidan Li, Xinmiao Jia, Chuan Qin, Tingting Yang, Lifeng Wang, Xiaoyuan Jiang, Nan Ding, Xiuli Zhang, Liya Yue, Zhe Yin, Lijun Zeng, Yongliang Zhao, Dongsheng Zhou, Fei Chen
- SUSCEPTIBILITY**
- Biocide Exposure Induces Changes in Susceptibility, Pathogenicity, and Biofilm Formation in Uropathogenic *Escherichia coli*** e01892-18
E. L. Henly, J. A. R. Dowling, J. B. Maingay, M. M. Lacey, T. J. Smith, S. Forbes
- Detection of Echinocandin-Resistant *Candida glabrata* in Blood Cultures Spiked with Different Percentages of *FKS2* Mutants** e02004-18
María Ángeles Bordallo-Cardona, Carlos Sánchez-Carrillo, Emilio Bouza, Patricia Muñoz, Pilar Escribano, Jesús Guinea
- A Rapid Unraveling of the Activity and Antibiotic Susceptibility of Mycobacteria** e02194-18
A. Mustazzolu, L. Venturelli, S. Dinarelli, K. Brown, R. A. Floto, G. Dietler, L. Fattorini, S. Kasas, M. Girasole, G. Longo
- Turning the Tide against Antibiotic Resistance by Evaluating Novel, Halogenated Phenazine, Quinoline, and NH125 Compounds against *Ureaplasma* Species Clinical Isolates and *Mycoplasma* Type Strains** e02265-18
Marissa A. Valentine-King, Katherine Cisneros, Margaret O. James, Robert W. Huigens III, Mary B. Brown
- High Prevalence of Bedaquiline Resistance in Treatment-Naive Tuberculosis Patients and Verapamil Effectiveness** e02530-18
Hasan Ghajavand, Mansour Kargarpour Kamakoli, Sharareh Khanipour, Shahin Pourazar Dizaji, Morteza Masoumi, Fatemeh Rahimi Jamnani, Abolfazl Fateh, Seyed Davar Siadat, Farzam Vaziri
- In Vitro* Activity of the New β -Lactamase Inhibitors Relebactam and Vaborbactam in Combination with β -Lactams against *Mycobacterium abscessus* Complex Clinical Isolates** e02623-18
Amit Kaushik, Nicole C. Ammerman, Jin Lee, Olumide Martins, Barry N. Kreiswirth, Gyanu Lamichhane, Nicole M. Parrish, Eric L. Nuermberger
- ANTIVIRAL AGENTS**
- Relationship of Ganciclovir Therapeutic Drug Monitoring with Clinical Efficacy and Patient Safety** e01855-18
Brianne M. Ritchie, Jason N. Barreto, Erin F. Barreto, Stacy A. Crow, Ross A. Dierkhising, Paul J. Jannetto, Pritish K. Tosh, Raymund R. Razonable
- Endonuclease Activity Inhibition of the NS1 Protein of Parvovirus B19 as a Novel Target for Antiviral Drug Development** e01879-18
Peng Xu, Safder S. Ganaie, Xiaomei Wang, Zekun Wang, Steve Kleiboeker, Nancy C. Horton, Richard F. Heier, Marvin J. Meyers, John E. Tavis, Jianming Qiu

- Pharmacokinetics of Dapivirine Transfer into Blood Plasma, Breast Milk, and Cervicovaginal Fluid of Lactating Women Using the Dapivirine Vaginal Ring** e01930-18
Lisa M. Noguchi, Craig Hoesley, Cliff Kelly, Rachel Scheckter, Katherine Bunge, Annalene Nel, Mark A. Marzinke, Craig W. Hendrix, Charlene S. Dezzutti, Sharon L. Hillier, Debra L. Bogen, Jeanna M. Piper, Richard H. Beigi
- Viral RNA-Dependent RNA Polymerase Inhibitor 7-Deaza-2'-C-Methyladenosine Prevents Death in a Mouse Model of West Nile Virus Infection** e02093-18
Luděk Eyer, Martina Fojtíková, Radim Nencka, Ivo Rudolf, Zdeněk Hubálek, Daniel Ruzek
- Barrier to Resistance of Dolutegravir in Two-Drug Combinations** e02104-18
Tomokazu Yoshinaga, Shigeru Miki, Shinobu Kawauchi-Miki, Takahiro Seki, Tamio Fujiwara
- Use of Letemovir as Salvage Therapy for Drug-Resistant Cytomegalovirus Retinitis** e02337-18
Nicholas Turner, Andrew Strand, Dilraj S. Grewal, Gary Cox, Sana Arif, Arthur W. Baker, Eileen K. Maziarz, Jennifer H. Saullo, Cameron R. Wolfe
- EPIDEMIOLOGY AND SURVEILLANCE**
- Understanding the Components, Calculation, and Impact of Monthly and Seasonal Variation of the Standardized Antimicrobial Utilization Ratio (SAAR)** e01780-18
Sean N. Avedissian, Nathaniel J. Rhodes, Jiajun Liu, Doaa Aljefri, Michael J. Postelnick, Sarah H. Sutton, Teresa R. Zembower, David Martin, Gwendolyn Pais, Caroline E. Cruce, Marc H. Scheetz
- Changing Molecular Markers of Antimalarial Drug Sensitivity across Uganda** e01818-18
Victor Asua, Joanna Vinden, Melissa D. Conrad, Jennifer Legac, Simon P. Kigozi, Moses R. Kanya, Grant Dorsey, Samuel L. Nsobya, Philip J. Rosenthal
- Spreading Patterns of NDM-Producing *Enterobacteriaceae* in Clinical and Environmental Settings in Yangon, Myanmar** e01924-18
Yo Sugawara, Yukihiko Akeda, Hideharu Hagiya, Noriko Sakamoto, Dan Takeuchi, Rathina Kumar Shanmugakani, Daisuke Motooka, Isao Nishi, Khwar Nyo Zin, Mya Mya Aye, Thuzar Myint, Kazunori Tomono, Shigeyuki Hamada
- Antimicrobial Activity of Omadacycline Tested against Clinical Bacterial Isolates from Hospitals in Mainland China, Hong Kong, and Taiwan: Results from the SENTRY Antimicrobial Surveillance Program (2013 to 2016)** e02262-18
Cecilia G. Carvalhaes, Michael D. Huband, Harald H. Reinhart, Robert K. Flamm, Helio S. Sader
- EXPERIMENTAL THERAPEUTICS**
- Direct and Indirect Inhibition Effects of Resveratrol against *Toxoplasma gondii* Tachyzoites *In Vitro*** e01233-18
Qi-Wei Chen, Kai Dong, Han-Xiao Qin, Yi-Kai Yang, Jin-Lei He, Jiao Li, Zhi-Wan Zheng, Da-Li Chen, Jian-Ping Chen
- Small-Molecule Inhibitor of FosA Expands Fosfomycin Activity to Multidrug-Resistant Gram-Negative Pathogens** e01524-18
Adam D. Tomich, Erik H. Klontz, Daniel Deredge, John P. Barnard, Christi L. McElheny, Megan L. Eshbach, Ora A. Weisz, Patrick Wintrobe, Yohei Doi, Eric J. Sundberg, Nicolas Sluis-Cremer

- Pharmacokinetics and Pharmacodynamics of Murepavadin in Neutropenic Mouse Models** e01699-18
M. J. Melchers, J. Teague, P. Warn, J. Hansen, F. Bernardini, A. Wach, D. Obrecht, G. E. Dale, J. W. Mouton
- In Vitro and In Vivo Studies of Spironolactone as an Antischistosomal Drug Capable of Clinical Repurposing** e01722-18
Rafael A. Guerra, Marcos P. Silva, Tais C. Silva, Maria C. Salvadori, Fernanda S. Teixeira, Rosimeire N. de Oliveira, Jefferson A. Rocha, Pedro L. S. Pinto, Josué de Moraes
- Structure-Activity Relationships of Wollamide Cyclic Hexapeptides with Activity against Drug-Resistant and Intracellular *Mycobacterium tuberculosis*** e01773-18
Zeinab G. Khalil, Timothy A. Hill, Luis M. De Leon Rodriguez, Rink-Jan Lohman, Huy N. Hoang, Norbert Reiling, Doris Hillemann, Margaret A. Brimble, David P. Fairlie, Antje Blumenthal, Robert J. Capon
- Evaluation of 4-Amino 2-Anilinoquinazolines against *Plasmodium* and Other Apicomplexan Parasites *In Vitro* and in a *P. falciparum* Humanized NOD-scid IL2R γ ^{null} Mouse Model of Malaria** e01804-18
Paul R. Gilson, William Nguyen, William A. Poole, Jose E. Teixeira, Jennifer K. Thompson, Kaiyuan Guo, Rebecca J. Stewart, Trent D. Ashton, Karen L. White, Laura M. Sanz, Francisco-Javier Gamo, Susan A. Charman, Sergio Wittlin, James Duffy, Christopher J. Tonkin, Wai-Hong Tham, Brendan S. Crabb, Brian M. Cooke, Christopher D. Huston, Alan F. Cowman, Brad E. Sleebs
- Oxazolidinones Can Replace Clarithromycin in Combination with Rifampin in a Mouse Model of Buruli Ulcer** e02171-18
Deepak V. Almeida, Till F. Omansen, Si-Yang Li, Jin Lee, Jacques H. Grosset, Paul J. Converse, Eric L. Nuermberger
- Rufomycin Targets ClpC1 Proteolysis in *Mycobacterium tuberculosis* and *M. abscessus*** e02204-18
Mary P. Choules, Nina M. Wolf, Hyun Lee, Jeffrey R. Anderson, Edyta M. Grzelak, Yuehong Wang, Rui Ma, Wei Gao, James B. McAlpine, Ying-Yu Jin, Jinhua Cheng, Hanki Lee, Joo-Won Suh, Nguyen Minh Duc, Seungwha Paik, Jin Ho Choe, Eun-Kyeong Jo, Chulhun L. Chang, Jong Seok Lee, Birgit U. Jaki, Guido F. Pauli, Scott G. Franzblau, Sanghyun Cho
- The Fungal Cyp51-Specific Inhibitor VT-1598 Demonstrates *In Vitro* and *In Vivo* Activity against *Candida auris*** e02233-18
Nathan P. Wiederhold, Shawn R. Lockhart, Laura K. Najvar, Elizabeth L. Berkow, Rosie Jaramillo, Marcos Olivo, Edward P. Garvey, Christopher M. Yates, Robert J. Schotzinger, Gabriel Catano, Thomas F. Patterson
- Structure, Mechanism, and Inhibition of *Aspergillus fumigatus* Thioredoxin Reductase** e02281-18
Andrew C. Marshall, Sarah E. Kidd, Stephanie J. Lamont-Friedrich, Georgia Arentz, Peter Hoffmann, Bryan R. Coad, John B. Bruning
- Screening the Pathogen Box for Identification of New Chemical Agents with Anti-*Fasciola hepatica* Activity** e02373-18
Claudia Machicado, Maria Pia Soto, Olga Timoteo, Abraham Vaisberg, Monica Pajuelo, Pedro Ortiz, Luis A. Marcos

- Pharmacokinetic/Pharmacodynamic Evaluation of a Novel Aminomethylcycline Antibiotic, KBP-7072, in the Neutropenic Murine Pneumonia Model against *Staphylococcus aureus* and *Streptococcus pneumoniae*** e02404-18
Alexander J. Lepak, Miao Zhao, Qingmei Liu, Ping Wang, Yanli Wang, Justin C. Bader, Paul G. Ambrose, David R. Andes

CLINICAL THERAPEUTICS

- The Hypothetical Impact of Accelerate Pheno on Time to Effective Therapy and Time to Definitive Therapy for Bloodstream Infections Due to Drug-Resistant Gram-Negative Bacilli** e01477-18
Oryan Henig, Keith S. Kaye, Suganya Chandramohan, Christopher C. Cooper, Paul Lephart, Hossein Salimnia, Maureen Taylor, Jason M. Pogue

- Bone and Joint Tissue Penetration of the *Staphylococcus*-Selective Antibiotic Afabicin in Patients Undergoing Elective Hip Replacement Surgery** e01669-18
Annick Menetrey, Annick Janin, John Pullman, J. Scott Overcash, Amina Haouala, François Leylaverigne, Laurent Turbe, Frederick Wittke, Valérie Nicolas-Métral

- Linezolid Pharmacokinetics in South African Patients with Drug-Resistant Tuberculosis and a High Prevalence of HIV Coinfection** e02164-18
Sean Wasserman, Paolo Denti, James C. M. Brust, Mahmoud Abdelwahab, Siphokazi Hlungulu, Lubbe Wiesner, Jennifer Norman, Frederick A. Sirgel, Robin M. Warren, Aliasgar Esmail, Keertan Dheda, Neel R. Gandhi, Graeme Meintjes, Gary Maartens

- A First-in-Human Safety, Tolerability, and Pharmacokinetics Study of Benapenem in Healthy Chinese Volunteers** e02188-18
Cai-Yun Zhao, Yuan Lv, Yan Zhu, Min-Ji Wei, Meng-Ying Liu, Xi-Wei Ji, Zi-Sheng Kang, Ya-Hong Xia, Ji-Hong Tian, Yan Ma, Yan Liu

- Adjuvant β -Lactam Therapy Combined with Vancomycin for Methicillin-Resistant *Staphylococcus aureus* Bacteremia: Does β -Lactam Class Matter?** e02211-18
Thomas J. Dilworth, Anthony M. Casapao, Omar M. Ibrahim, David M. Jacobs, Dana R. Bowers, Nicholas D. Beyda, Renee-Claude Mercier

- Isavuconazole in the Treatment of Coccidioidal Meningitis** e02232-18
Arash Heidari, Miriam Quinlan, David J. Benjamin, Brett Laurence, Anandit Mu, Tiffany Ngai, Wes J. Hoffman, Stuart H. Cohen, Ian McHardy, Royce Johnson, George R. Thompson III

- Efficacy and Safety of Pyronaridine-Artesunate plus Single-Dose Primaquine for Treatment of Uncomplicated *Plasmodium falciparum* Malaria in Eastern Cambodia** e02242-18
Rithea Leang, Melissa Mairet-Khedim, Huch Chea, Rekol Huy, Nimol Khim, Denis Mey Bouth, Maria Dorina Bustos, Pascal Ringwald, Benoit Witkowski

PHARMACOLOGY

- Pharmacokinetic Data Are Predictive of *In Vivo* Efficacy for Cefixime and Ceftriaxone against Susceptible and Resistant *Neisseria gonorrhoeae* Strains in the Gonorrhea Mouse Model** e01644-18
Kristie L. Connolly, Ann E. Eakin, Carolina Gomez, Blaire L. Osborn, Magnus Unemo, Ann E. Jerse

- Mass Balance and Drug Interaction Potential of Intravenous Eravacycline Administered to Healthy Subjects** e01810-18
Joseph V. Newman, Jian Zhou, Sergey Izmailyan, Larry Tsai

Are Standard Dosing Regimens of Ceftriaxone Adapted for Critically Ill Patients with Augmented Creatinine Clearance? e02134-18

Julien Ollivier, Cédric Carrié, Nicolas d'Houdain, Sarah Djabarouti, Laurent Petit, Fabien Xuereb, Rachel Legeron, Matthieu Biais, Dominique Breilh

Dose-Dependent Synergistic Interactions of Colistin with Rifampin, Meropenem, and Tigecycline against Carbapenem-Resistant *Klebsiella pneumoniae* Biofilms e02357-18

Anastasia Geladari, Maria Simitsopoulou, Charalampos Antachopoulos, Emmanuel Roilides

LETTERS TO THE EDITOR

Ceftolozane-Tazobactam Pharmacokinetics during Extracorporeal Membrane Oxygenation in a Lung Transplant Recipient e02131-18

Fabio Arena, Luca Marchetti, Lucia Henrici De Angelis, Enivarco Maglioni, Martina Contorni, Maria Iris Cassetta, Andrea Novelli, Gian Maria Rossolini

Small IncQ1 and Col-Like Plasmids Harboring *bla*_{KPC-2} and Non-Tn4401 Elements (NTE_{KPC-1IId}) in High-Risk Lineages of *Klebsiella pneumoniae* CG258 e02140-18

Louise T. Cerdeira, Margaret M. C. Lam, Kelly L. Wyres, Ryan R. Wick, Louise M. Judd, Ralf Lopes, Rosineide M. Ribas, Marcia M. Morais, Kathryn E. Holt, Nilton Lincopan

Detection of *mcr*-Mediated Colistin Resistance in *Escherichia coli* Isolates from Pigs in Small-Scale Farms in Cambodia e02241-18

G. Ström Hallenberg, S. Börjesson, S. Sokerya, T. Sothyra, U. Magnusson